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#### (57) Abstract

Various molecules associated with cancer are disclosed. The invention also discloses diagnostic and therapeutic methods based upon these molecules.

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#### CANCER ASSOCIATED NUCLEIC ACIDS AND POLYPEPTIDES

#### Field of the Invention

The invention relates to nucleic acids and encoded polypeptides which are cancer

associated antigens expressed in patients afflicted with breast cancer. The invention also relates
to agents which bind the nucleic acids or polypeptides. The nucleic acid molecules,
polypeptides coded for by such molecules and peptides derived therefrom, as well as related
antibodies and cytolytic T lymphocytes, are useful, *inter alia*, in diagnostic and therapeutic
contexts.

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#### **Background of the Invention**

The mechanism by which T cells recognize foreign materials has been implicated in cancer. A number of cytolytic T lymphocyte (CTL) clones directed against autologous melanoma antigens, testicular antigens, and melanocyte differentiation antigens have been described. In many instances, the antigens recognized by these clones have been characterized.

The use of autologous CTLs for identifying tumor antigens requires that the target cells which express the antigens can be cultured *in vitro* and that stable lines of autologous CTL clones which recognize the antigen-expressing cells can be isolated and propagated. While this approach has worked well for melanoma antigens, other tumor types, such as epithelial cancers including breast and colon cancer, have proved refractory to the approach.

More recently another approach to the problem has been described by Sahin et al. (*Proc. Natl. Acad. Sci. USA* 92:11810-11813, 1995). According to this approach, autologous antisera are used to identify immunogenic protein antigens expressed in cancer cells by screening expression libraries constructed from tumor cell cDNA. Antigen-encoding clones so identified have been found to have elicited an high-titer humoral immune response in the patients from which the antisera were obtained. Such a high-titer IgG response implies helper T cell recognition of the detected antigen. These tumor antigens can then be screened for the presence of MHC/HLA class I and class II motifs and reactivity with CTLs

The invention is elaborated upon in the disclosure which follows.

#### Summary f the Invention

Autologous antibody screening has now been applied to cancer using antisera from cancer patients. Numerous cancer associated antigens have been identified. The invention provides, *inter alia*, isolated nucleic acid molecules, expression vectors containing those molecules and host cells transfected with those molecules. The invention also provides isolated proteins and peptides, antibodies to those proteins and peptides and CTLs which recognize the proteins and peptides. Fragments including functional fragments and variants of the foregoing also are provided. Kits containing the foregoing molecules additionally are provided. The foregoing can be used in the diagnosis, monitoring, research, or treatment of conditions characterized by the expression of one or more cancer associated antigens.

Prior to the present invention, only a handful of cancer associated genes had been identified in the past 20 years. The invention involves the surprising discovery of many genes, some previously known and many previously unknown, which are expressed in individuals who have cancer. These individuals all have serum antibodies against the proteins (or fragments thereof) encoded by these genes. Thus, abnormally expressed genes are recognized by the host's immune system and therefore can form a basis for diagnosis, monitoring and therapy.

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The invention involves the use of a single material, a plurality of different materials and even large panels and combinations of materials. For example, a single gene, a single protein encoded by a gene, a single functional fragment thereof, a single antibody thereto, etc. can be used in methods and products of the invention. Likewise, pairs, groups and even panels of these materials can be used for diagnosis, monitoring and therapy. The pairs, groups or panels can involve 2, 3, 4, 5... to as many as 25, 50, 100 or more genes, gene products, fragments thereof or agents that recognize such materials. A plurality of such materials are not only useful in monitoring, typing, characterizing and diagnosing cells abnormally expressing such genes, but a plurality of such materials can be used therapeutically. An example of the use of a plurality of such materials for the prevention, delay of onset, amelioration, etc. of cancer cells, which express or will express such genes prophylactically or acutely. Any and all combinations of the genes, gene products, and materials which recognize the genes and gene products can be tested and identified for use according to the invention. It would be far too lengthy to recite all such combinations; those skilled in the art, particularly in view of the teaching contained herein, will readily be able to determine which combinations are most appropriate for which circumstances.

As will be clear from the following discussion, the invention has in vivo and in vitro uses,

including for therapeutic, diagnostic, monitoring and research purposes. One aspect of the invention is the ability to fingerprint a cell expressing a number of the genes identified according to the invention. Such fingerprints will be characteristic, for example, of the stage of the cancer, the type of the cancer, or even the effect in animal models of a therapy on a cancer. Cells also can be screened to determine whether such cells abnormally express the genes identified according to the invention.

The invention, in one aspect, is a method of diagnosing a disorder characterized by expression of a cancer associated antigen precursor coded for by a nucleic acid molecule. The method involves the steps of contacting a biological sample isolated from a subject with an agent that specifically binds to the nucleic acid molecule, an expression product thereof, or a fragment of an expression product thereof complexed with an MHC, preferably an HLA, molecule, wherein the nucleic acid molecule is a NA Group 1 nucleic acid molecule, and determining the interaction between the agent and the nucleic acid molecule, the expression product or fragment of the expression product as a determination of the disorder.

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In one embodiment the agent is selected from the group consisting of (a) a nucleic acid molecule comprising NA Group 1 nucleic acid molecules or a fragment thereof, (b) a nucleic acid molecule comprising NA Group 3 nucleic acid molecules or a fragment thereof, (c) a nucleic acid molecule comprising NA Group 17 nucleic acid molecules or a fragment thereof, (d) an antibody that binds to an expression product, or a fragment thereof, of NA group 1 nucleic acids, (e) an antibody that binds to an expression product, or a fragment thereof, of NA group 3 nucleic acids, (f) an antibody that binds to an expression product, or a fragment thereof, of NA group 17 nucleic acids, (g) and agent that binds to a complex of an MHC, preferably HLA, molecule and a fragment of an expression product of a NA Group 1 nucleic acid, (h) an agent that binds to a complex of an MHC, preferably HLA, molecule and a fragment of an expression product of a NA group 3 nucleic acid, and (I) an agent that binds to a complex of an MHC, preferably HLA, molecule and a fragment of an expression product of a NA Group 17 nucleic acid.

The disorder may be characterized by expression of a plurality of cancer associated antigen precursors and wherein the agent is a plurality of agents, each of which is specific for a different human cancer associated antigen precursor, and wherein said plurality of agents is at least 2, at least 3, at least 4, at least 5, at least 6, at least 7, at least 8, at least 9 or at least 10 such agents.

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In each of the above embodiments the agent may be specific for a human cancer associated antigen precursor that is a breast, a gastric, a lung, a prostate, a renal or a colon cancer associated antigen precursor.

In another aspect the invention is a method for determining regression, progression or onset of a condition characterized by expression of abnormal levels of a protein encoded by a nucleic acid molecule that is a NA Group 1 molecule. The method involves the steps of monitoring a sample, from a subject who has or is suspected of having the condition, for a parameter selected from the group consisting of (i) the protein, (ii) a peptide derived from the protein, (iii) an antibody which selectively binds the protein or peptide, and (iv) cytolytic T cells specific for a complex of the peptide derived from the protein and an MHC molecule, as a determination of regression, progression or onset of said condition. In one embodiment the sample is a body fluid, a body effusion or a tissue.

In another embodiment the step of monitoring comprises contacting the sample with a detectable agent selected from the group consisting of (a) an antibody which selectively binds the protein of (i), or the peptide of (ii), (b) a protein or peptide which binds the antibody of (iii), and (c) a cell which presents the complex of the peptide and MHC molecule of (iv). In a preferred embodiment the antibody, the protein, the peptide or the cell is labeled with a radioactive label or an enzyme. The sample in a preferred embodiment is assayed for the peptide.

According to another embodiment the nucleic acid molecule is one of the following: a NA Group 3 molecule, a NA Group 11 molecule, a NA Group 12 molecule, a NA Group 13 molecule, a NA Group 14 molecule, a NA Group 15 molecule, or a NA Group 16 molecule. In yet another embodiment the protein is a plurality of proteins, the parameter is a plurality of parameters, each of the plurality of parameters being specific for a different of the plurality of proteins.

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The invention in another aspect is a pharmaceutical preparation for a human subject. The pharmaceutical preparation includes an agent which when administered to the subject enriches selectively the presence of complexes of an HLA molecule and a human cancer associated antigen, and a pharmaceutically acceptable carrier, wherein the human cancer associated antigen is a fragment of a human cancer associated antigen precursor encoded by a nucleic acid molecule which comprises a NA Group 1 molecule. In one embodiment the nucleic acid molecule is a NA Group 3 nucleic acid molecule.

The agent in one embodiment comprises a plurality of agents, each of which enriches selectively in the subject complexes of an HLA molecule and a different human cancer associated antigen. Preferably the plurality is at least two, at least three, at least four or at least 5 different such agents.

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In another embodiment the agent is selected from the group consisting of (1) an isolated polypeptide comprising the human cancer associated antigen, or a functional variant thereof, (2) an isolated nucleic acid operably linked to a promoter for expressing the isolated polypeptide, or functional variant thereof, (3) a host cell expressing the isolated polypeptide, or functional variant thereof, and (4) isolated complexes of the polypeptide, or functional variant thereof, and an HLA molecule.

The agent may be a cell expressing an isolated polypeptide. In one embodiment the agent is a cell expressing an isolated polypeptide comprising the human cancer associated antigen or a functional variant thereof, and wherein the cell is nonproliferative. In another embodiment the agent is a cell expressing an isolated polypeptide comprising the human cancer associated antigen or a functional variant thereof, and wherein the cell expresses an HLA molecule that binds the polypeptide. The cell can express one or both of the polypeptide and HLA molecule recombinantly. In another preferred embodiment the cell is nonproliferative. In yet another embodiment the agent is at least two, at least three, at least four or at least five different polypeptides, each representing a different human cancer associated antigen or functional variant thereof.

The agent in one embodiment is a PP Group 2 polypeptide. In other embodiments the agent is a PP Group 3 polypeptide or a PP Group 4 polypeptide.

In an embodiment each of the pharmaceutical preparations described herein also includes an adjuvant.

According to another aspect the invention, a composition is provided of an isolated agent that binds selectively a PP Group 1 polypeptide. In separate embodiments the agent binds selectively to a polypeptide selected from the following: a PP Group 3 polypeptide, a PP Group 11 polypeptide, a PP Group 12 polypeptide, a PP Group 13 polypeptide, a PP Group 14 polypeptide, a PP Group 15 polypeptide, and a PP Group 16 polypeptide. In other embodiments, the agent is a plurality of different agents that bind selectively at least two, at least three, at least four, or at least five different such polypeptides. In each of the above described embodiments the agent may be an antibody.

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In another aspect the invention is a composition of matter .composed of a conjugate of the agent of the above-described compositions of the invention and a therapeutic or diagnostic agent. Preferably the conjugate is of the agent and a therapeutic or diagnostic that is an antineoplastic.

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The invention in another aspect is a pharmaceutical composition of an isolated nucleic acid molecule selected from the group consisting of: (1) NA Group 1 molecules, and (2) NA Group 2 molecules, and a pharmaceutically acceptable carrier. In one embodiment the isolated nucleic acid molecule comprises a NA Group 3 or NA Group 4 molecule. In another embodiment the isolated nucleic acid molecule comprises at least two isolated nucleic acid molecules coding for two different polypeptides, each polypeptide comprising a different cancer associated antigen.

Preferably the pharmaceutical composition also includes an expression vector with a promoter operably linked to the isolated nucleic acid molecule. In another embodiment the pharmaceutical composition also includes a host cell recombinantly expressing the isolated nucleic acid molecule.

According to another aspect of the invention a pharmaceutical composition is provided. The pharmaceutical composition includes an isolated polypeptide comprising a PP Group 1 or a PP Group 2 polypeptide, and a pharmaceutically acceptable carrier. In one embodiment the isolated polypeptide comprises a PP Group 3 or a PP Group 4 polypeptide.

In another embodiment the isolated polypeptide comprises at least two different polypeptides, each comprising a different cancer associated antigen. In separate embodiments the isolated polypeptides are selected from the following: PP Group 11 polypeptides or HLA binding fragments thereof, PP Group 12 polypeptides or HLA binding fragments thereof, PP Group 13 polypeptides or HLA binding fragments thereof, PP Group 14 polypeptides or HLA binding fragments thereof, or PP Group 16 polypeptides or HLA binding fragments thereof.

In an embodiment each of the pharmaceutical compositions described herein also includes an adjuvant.

Another aspect the invention is an isolated nucleic acid molecule comprising a NA Group 3 molecule. Another aspect the invention is an isolated nucleic acid molecule comprising a NA Group 4 molecule. In separate embodiments the isolated nucleic acid molecules are selected from the following: a Group 11 molecule or a functional fragment

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thereof, a Group 12 molecule or a functional fragment thereof, a Group 13 molecule or a functional fragment thereof, a Group 14 molecule or a functional fragment thereof, a Group 15 molecule or a functional fragment thereof, or a Group 16 molecule or a functional fragment thereof.

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The invention in another aspect is an isolated nucleic acid molecule selected from the group consisting of (a) a fragment of a nucleic acid selected from the group of nucleic acid molecules consisting of SEQ ID numbered below and comprising all nucleic acid sequences among SEQ ID NOs 1-816, of sufficient length to represent a sequence unique within the human genome, and identifying a nucleic acid encoding a human cancer associated antigen precursor, (b) complements of (a), provided that the fragment includes a sequence of contiguous nucleotides which is not identical to any sequence selected from the sequence group consisting of (1) sequences having the GenBank accession numbers of the sequence Group 1, (2) complements of (1), and (3) fragments of (1) and (2).

In one embodiment the sequence of contiguous nucleotides is selected from the group consisting of: (1) at least two contiguous nucleotides nonidentical to the sequence Group 1, (2) at least three contiguous nucleotides nonidentical to the sequence Group 1, (3) at least four contiguous nucleotides nonidentical to the sequence Group 1, (4) at least five contiguous nucleotides nonidentical to the sequence Group 1, (5) at least six contiguous nucleotides nonidentical to the sequence Group 1, or (6) at least seven contiguous nucleotides nonidentical to the sequence Group 1.

In another embodiment the fragment has a size selected from the group consisting of at least: 8 nucleotides, 10 nucleotides, 12 nucleotides, 14 nucleotides, 16 nucleotides, 18 nucleotides, 20, nucleotides, 22 nucleotides, 24 nucleotides, 26 nucleotides, 28 nucleotides, 30 nucleotides, 50 nucleotides, 75 nucleotides, 100 nucleotides, 200 nucleotides, 1000 nucleotides and every integer length therebetween.

In yet another embodiment the molecule encodes a polypeptide which, or a fragment of which, binds a human HLA receptor or a human antibody.

Another aspect of the invention is an expression vector comprising an isolated nucleic acid molecule of the invention described above operably linked to a promoter.

According to one aspect the invention is an expression vector comprising a nucleic acid operably linked to a promoter, wherein the nucleic acid is a NA Group 2 molecule. In another aspect the invention is an expression vector comprising a NA Group 1 or Group 2 molecule

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and a nucleic acid encoding an MHC, preferably HLA, molecule.

In yet another aspect the invention is a host cell transformed or transfected with an expression vector of the invention described above.

In another aspect the invention is a host cell transformed or transfected with an expression vector comprising an isolated nucleic acid molecule of the invention described above operably linked to a promoter, or an expression vector comprising a nucleic acid operably linked to a promoter, wherein the nucleic acid is a NA Group 1 or 2 molecule and further comprising a nucleic acid encoding HLA.

According to another aspect of the invention an isolated polypeptide encoded by the isolated nucleic acid molecules the invention, described above, is provided. These include PP Group 1-17 polypeptides. The invention also includes a fragment of the polypeptide which is immunogenic. In one embodiment the fragment, or a portion of the fragment, binds HLA or a human antibody.

The invention includes in another aspect an isolated fragment of a human cancer associated antigen precursor which, or portion of which, binds HLA or a human antibody, wherein the precursor is encoded by a nucleic acid molecule that is a NA Group 1 molecule. In one embodiment the fragment is part of a complex with HLA. In another embodiment the fragment is between 8 and 12 amino acids in length. In another embodiment the invention includes an isolated polypeptide comprising a fragment of the polypeptide of sufficient length to represent a sequence unique within the human genome and identifying a polypeptide that is a human cancer associated antigen precursor.

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According to another aspect of the invention a kit for detecting the presence of the expression of a cancer associated antigen precursor is provided. The kit includes a pair of isolated nucleic acid molecules each of which consists essentially of a molecule selected from the group consisting of (a) a 12-32 nucleotide contiguous segment of the nucleotide sequence of any of the NA Group 1 molecules and (b) complements of ("a"), wherein the contiguous segments are nonoverlapping. In one embodiment the pair of isolated nucleic acid molecules is constructed and arranged to selectively amplify an isolated nucleic acid molecule that is a NA Group 3 molecule. Preferably, the pair amplifies a human NA Group 3 molecule.

According to another aspect of the invention a method for treating a subject with a disorder characterized by expression of a human cancer associated antigen precursor is provided. The method includes the step of administering to the subject an amount of an agent,

which enriches selectively in the subject the presence of complexes of an HLA molecule and a human cancer associated antigen, effective to ameliorate the disorder, wherein the human cancer associated antigen is a fragment of a human cancer associated antigen precursor encoded by a nucleic acid molecule selected from the group consisting of (a) a nucleic acid molecule comprising NA group 1 nucleic acid molecules, (b) a nucleic acid molecule comprising NA group 3 nucleic acid molecules, (c) a nucleic acid molecule comprising NA group 17 nucleic acid molecules.

In one embodiment the disorder is characterized by expression of a plurality of human cancer associated antigen precursors and wherein the agent is a plurality of agents, each of which enriches selectively in the subject the presence of complexes of an HLA molecule and a different human cancer associated antigen. Preferably the plurality is at least 2, at least 3, at least 4, or at least 5 such agents.

In another embodiment the agent is an isolated polypeptide selected from the group consisting of PP Group 1, PP Group 2, PP Group 3, PP Group 4, PP Group 5, PP Group 6, PP Group 7, PP Group 8, PP Group 9, PP Group 10, PP Group 11, PP Group 12, PP Group 13, PP Group 14, PP Group 15, PP Group 16 and PP Group 17 polypeptides.

In yet another embodiment the disorder is cancer.

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According to another aspect the invention is a method for treating a subject having a condition characterized by expression of a cancer associated antigen precursor in cells of the subject. The method includes the steps of (I) removing an immunoreactive cell containing sample from the subject, (ii) contacting the immunoreactive cell containing sample to the host cell under conditions favoring production of cytolytic T cells against a human cancer associated antigen which is a fragment of the precursor, (iii) introducing the cytolytic T cells to the subject in an amount effective to lyse cells which express the human cancer associated antigen, wherein the host cell is transformed or transfected with an expression vector comprising an isolated nucleic acid molecule operably linked to a promoter, the isolated nucleic acid molecule being selected from the group of nucleic acid molecules consisting of NA Group 1, NA Group 2, NA Group 3, NA Group 4, NA Group 5, NA Group 6, NA Group 7, NA Group 8, NA Group 9, NA Group 10, NA Group 11, NA Group 12, NA Group 13, NA Group 14, NA Group 15, NA Group 16, and NA Group 17.

In one embodiment the host cell recombinantly expresses an HLA molecule which binds the human cancer associated antigen. In another embodiment the host cell endogenously

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expresses an HLA molecule which binds the human cancer associated antigen.

The invention includes in another aspect a method for treating a subject having a condition characterized by expression of a cancer associated antigen precursor in cells of the subject. The method includes the steps of (I) identifying a nucleic acid molecule expressed by the cells associated with said condition, wherein said nucleic acid molecule is a NA Group 1 molecule (ii) transfecting a host cell with a nucleic acid selected from the group consisting of (a) the nucleic acid molecule identified, (b) a fragment of the nucleic acid identified which includes a segment coding for a cancer associated antigen, (c) deletions, substitutions or additions to (a) or (b), and (d) degenerates of (a), (b), or (c); (iii) culturing said transfected host cells to express the transfected nucleic acid molecule, and; (iv) introducing an amount of said host cells or an extract thereof to the subject effective to increase an immune response against the cells of the subject associated with the condition. Preferably, the antigen is a human antigen and the subject is a human.

In one embodiment the method also includes the step of (a) identifying an MHC molecule which presents a portion of an expression product of the nucleic acid molecule, wherein the host cell expresses the same MHC molecule as identified in (a) and wherein the host cell presents an MHC binding portion of the expression product of the nucleic acid molecule.

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In another embodiment the method also includes the step of treating the host cells to render them non-proliferative.

In yet another embodiment the immune response comprises a B-cell response or a T cell response. Preferably the response is a T-cell response which comprises generation of cytolytic T-cells specific for the host cells presenting the portion of the expression product of the nucleic acid molecule or cells of the subject expressing the human cancer associated antigen.

In another embodiment the nucleic acid molecule is a NA Group 3 molecule.

Another aspect of the invention is a method for treating or diagnosing or monitoring a subject having a condition characterized by expression of an abnormal amount of a protein encoded by a nucleic acid molecule that is a NA Group 1 molecule. The method includes the step of administering to the subject an antibody which specifically binds to the protein or a peptide derived therefrom, the antibody being coupled to a therapeutically useful agent, in an amount effective to treat the condition.

In one embodiment the antibody is a monoclonal antibody. Preferably the monoclonal antibody is a chimeric antibody or a humanized antibody.

In another aspect the invention is a method for treating a condition characterized by expression in a subject of abnormal amounts of a protein encoded by a nucleic acid molecule that is a NA Group 1 nucleic acid molecule. The method involves the step of administering to a subject at least one of the pharmaceutical compositions of the invention described above in an amount effective to prevent, delay the onset of, or inhibit the condition in the subject. In one embodiment the condition is cancer. In another embodiment the method includes the step of first identifying that the subject expresses in a tissue abnormal amounts of the protein. The invention in another aspect is a method for treating a subject having a condition characterized by expression of abnormal amounts of a protein encoded by a nucleic acid molecule that is a NA Group 1 nucleic acid molecule. The method includes the steps of (I) identifying cells from the subject which express abnormal amounts of the protein; (ii) isolating a sample of the cells; (iii) cultivating the cells, and (iv) introducing the cells to the subject in an amount effective to provoke an immune response against the cells.

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In one embodiment the cells express a protein selected from the group consisting of a PP Group 11 protein, a PP Group 12 protein, a PP Group 13 protein, PP Group 14 protein, a PP Group 15 protein and a PP Group 16 protein. In another embodiment the method includes the step of rendering the cells non-proliferative, prior to introducing them to the subject.

In another aspect the invention is a method for treating a pathological cell condition characterized by abnormal expression of a protein encoded by a nucleic acid molecule that is a NA Group 1 nucleic acid molecule. The method includes the step of administering to a subject in need thereof an effective amount of an agent which inhibits the expression or activity of the protein.

In one embodiment the agent is an inhibiting antibody which selectively binds to the protein and wherein the antibody is a monoclonal antibody, a chimeric antibody or a humanized antibody. In another embodiment the agent is an antisense nucleic acid molecule which selectively binds to the nucleic acid molecule which encodes the protein. In yet another important embodiment the nucleic acid molecule is a NA Group 3 nucleic acid molecule.

The invention includes in another aspect a composition of matter useful in stimulating an immune response to a plurality of a protein encoded by nucleic acid molecules that are NA Group 1 molecules. The composition is a plurality of peptides derived from the amino acid

sequences of the proteins, wherein the peptides bind to one or more MHC molecules presented on the surface of the cells which express an abnormal amount of the protein.

In one embodiment at least a portion of the plurality of peptides bind to MHC molecules and elicit a cytolytic response thereto. In another embodiment the composition of matter includes an adjuvant. In another embodiment the adjuvant is a saponin, GM-CSF, or an interleukin.

According to another aspect the invention is an isolated antibody which selectively binds to a complex of: (I) a peptide derived from a protein encoded by a nucleic acid molecule that is a NA Group 1 molecule and (ii) and an MHC molecule to which binds the peptide to form the complex, wherein the isolated antibody does not bind to (I) or (ii) alone.

In one embodiment the antibody is a monoclonal antibody, a chimeric antibody or a humanized antibody.

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The invention also involves the use of the genes, gene products, fragments thereof, agents which bind thereto, and so on in the preparation of medicaments. A particular medicament is for treating cancer and a more particular medicament is for treating breast cancer, lung cancer, renal cancer, colon cancer, prostate cancer or gastric cancer.

#### **Detailed Description of the Invention**

In the above summary and in the ensuing description, lists of sequences are provided. The lists are meant to embrace each single sequence separately, two or more sequences together where they form a part of the same gene, any combination of two or more sequences which relate to different genes, including and up to the total number on the list, as if each and every combination were separately and specifically enumerated. Likewise, when mentioning fragment size, it is intended that a range embrace the smallest fragment mentioned to the full-length of the sequence (-1 so that it is a fragment), each and every fragment length intended as if specifically enumerated. Thus, if a fragment could be between 10 and 15 in length, it is explicitly meant to mean 10, 11, 12, 13, 14, or 15 in length.

The summary and the claims mention antigen precursors and antigens. As used in the summary and in the claims, a precursor is substantially the full-length protein encoded by the coding region of the isolated DNA and the antigen is a peptide which complexes with MHC, preferably HLA, and which participates in the immune response as part of that complex. Such antigens are typically 9 amino acids long, although this may vary slightly.

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As used herein, a subject is a human, non-human primate, cow, horse, pig, sheep, goat, dog, cat or rodent. In all embodiments human cancer antigens and human subjects are preferred.

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The present invention in one aspect involves the cloning of cDNAs encoding human cancer associated antigen precursors using autologous antisera of subjects having cancer. The sequences of the clones representing genes identified according to the methods described herein are presented in the attached Sequence Listing, and the predicted amino acid sequences of some clones also are presented. Of the foregoing, it can be seen that some of the clones are considered completely novel as no nucleotide or amino acid homologies to coding regions were found in the databases searched. Other clones are novel but have some homology to sequences deposited in databases (mainly EST sequences). Nevertheless, the entire gene sequence was not previously known. In some cases no function was suspected and in other cases, even if a function was suspected, it was not know that the gene was associated with cancer. In all cases, it was not known or suspected that the gene encoded a cancer antigen which reacted with antibody from autologous sera. Analysis of the clone sequences by comparison to nucleic acid and protein databases determined that still other of the clones surprisingly are closely related to other previously-cloned genes. The sequences of these related genes is also presented in the Sequence Listing. The nature of the foregoing genes as encoding antigens recognized by the immune systems of cancer patients is, of course, unexpected.

The invention thus involves in one aspect cancer associated antigen polypeptides, genes encoding those polypeptides, functional modifications and variants of the foregoing, useful fragments of the foregoing, as well as diagnostics and therapeutics relating thereto.

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Homologs and alleles of the cancer associated antigen nucleic acids of the invention can be identified by conventional techniques. Thus, an aspect of the invention is those nucleic acid sequences which code for cancer associated antigen precursors. Because this application contains so many sequences, the following chart is provided to identify the various groups of sequences discussed in the claims and in the summary:

### "Nucleic Acid Sequences"

NA Group 1. (a) nucleic acid molecules which hybridize under stringent conditions to a molecule consisting of a nucleic acid sequence selected from the group consisting of nucleic acid sequences among SEQ ID NOs 1-816 and which code for a cancer associated antigen precursor,

- (b) deletions, additions and substitutions which code for a respective cancer associated antigen precursor,
- (c) nucleic acid molecules that differ from the nucleic acid molecules of (a) or (b) in codon sequence due to the degeneracy of the genetic code, and
  - (d) complements of (a), (b) or (c).
- NA Group 2. Fragments of NA Group 1, which codes for a polypeptide which, or a portion of which, binds an MHC molecule to form a complex recognized by a an autologous antibody or lymphocyte.

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- NA Group 3. The subset of NA Group 1 where the nucleotide sequence is selected from the group consisting of:
- (a) previously unknown human nucleic acids coding for a human cancer associated antigen precursor,
- (b) deletions, additions and substitutions which code for a respective human cancer associated antigen precursor,
- (c) nucleic acid molecules that differ from the nucleic acid molecules of (a) or (b) in codon sequence due to the degeneracy of the genetic code, and
  - (d) complements of (a), (b) or (c).
- NA Group 4. Fragments of NA Group 3, which code for a polypeptide which, or a portion of which, binds to an MHC molecule to form a complex recognized by an autologous antibody or lymphocyte.
- NA Group 5. A subset of NA Group 1, wherein the nucleic acid molecule codes for a human breast cancer associated antigen precursor.
  - NA Group 6. A subset of NA Group 1, wherein the nucleic acid molecule codes for a human colon cancer associated antigen precursor.
- NA Group 7. A subset of NA Group 1, wherein the nucleic acid molecule codes for a human gastric cancer associated antigen precursor.

NA Group 8. A subset of NA Group 1, wherein the nucleic acid molecule codes for a human lung cancer associated antigen precursor.

NA Group 9. A subset of NA Group 1, wherein the nucleic acid molecule codes for a human renal cancer associated antigen precursor.

NA Group 10. A subset of NA Group 1, wherein the nucleic acid molecule codes for a human prostate cancer associated antigen precursor.

NA Group 11. A subset of NA Group 3, wherein the nucleic acid molecule codes for a human breast cancer associated antigen precursor.

NA Group 12. A subset of NA Group 3, wherein the nucleic acid molecule codes for a human colon cancer associated antigen precursor.

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NA Group 13. A subset of NA Group 3, wherein the nucleic acid molecule codes for a human gastric cancer associated antigen precursor.

NA Group 14. A subset of NA Group 3, wherein the nucleic acid molecule codes for a human lung cancer associated antigen precursor.

NA Group 15. A subset of NA Group 3, wherein the nucleic acid molecule codes for a human renal cancer associated antigen precursor.

NA Group 16. A subset of NA Group 3, wherein the nucleic acid molecule codes for a human prostate cancer associated antigen precursor.

NA Group 17. A subset of NA Group 1, comprising human cancer associated antigens that react with allogenic cancer antisera.

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#### Polypeptide Sequences

PP Group 1. Polypeptides encoded by NA Group 1.

- PP Group 2. Polypeptides encoded by NA Group 2
- PP Group 3. Polypeptides encoded by NA Group 3.
- PP Group 4. Polypeptides encoded by NA Group 4.
- PP Group 5. Polypeptides encoded by NA Group 5.
- 5 PP Group 6. Polypeptides encoded by NA Group 6.
  - PP Group 7. Polypeptides encoded by NA Group 7.
  - PP Group 8. Polypeptides encoded by NA Group 8.
  - PP Group 9. Polypeptides encoded by NA Group 9.
  - PP Group 10. Polypeptides encoded by NA Group 10.
- 10 PP Group 11. Polypeptides encoded by NA Group 11.
  - PP Group 12. Polypeptides encoded by NA Group 12.
  - PP Group 13. Polypeptides encoded by NA Group 13.
  - PP Group 14. Polypeptides encoded by NA Group 14.
  - PP Group 15. Polypeptides encoded by NA Group 15.
- 15 PP Group 16. Polypeptides encoded by NA Group 16.

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PP Group 17. Polypeptides encoded by NA Group 17.

The term "stringent conditions" as used herein refers to parameters with which the art is familiar. Nucleic acid hybridization parameters may be found in references which compile such methods, e.g. *Molecular Cloning: A Laboratory Manual*, J. Sambrook, et al., eds., Second Edition, Cold Spring Harbor Laboratory Press, Cold Spring Harbor, New York, 1989, or *Current Protocols in Molecular Biology*, F.M. Ausubel, et al., eds., John Wiley & Sons, Inc., New York. More specifically, stringent conditions, as used herein, refers, for example, to hybridization at 65°C in hybridization buffer (3.5 x SSC, 0.02% Ficoll, 0.02% polyvinyl pyrrolidone, 0.02% Bovine Serum Albumin, 2.5mM NaH<sub>2</sub>PO<sub>4</sub>(pH7), 0.5% SDS, 2mM EDTA). SSC is 0.15M sodium chloride/0.15M sodium citrate, pH7; SDS is sodium dodecyl sulphate; and EDTA is ethylenediaminetetracetic acid. After hybridization, the membrane upon which the DNA is transferred is washed, for example, in 2 x SSC at room temperature and then at 0.1 - 0.5 x SSC/0.1 x SDS at temperatures up to 68°C.

There are other conditions, reagents, and so forth which can be used, which result in a similar degree of stringency. The skilled artisan will be familiar with such conditions, and thus they are not given here. It will be understood, however, that the skilled artisan will be able to

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manipulate the conditions in a manner to permit the clear identification of homologs and alleles of cancer associated antigen nucleic acids of the invention (e.g., by using lower stringency conditions). The skilled artisan also is familiar with the methodology for screening cells and libraries for expression of such molecules which then are routinely isolated, followed by isolation of the pertinent nucleic acid molecule and sequencing.

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In general homologs and alleles typically will share at least 40% nucleotide identity and/or at least 50% amino acid identity to the sequences of breast cancer associated antigen nucleic acid and polypeptides, respectively, in some instances will share at least 50% nucleotide identity and/or at least 65% amino acid identity and in still other instances will share at least 60% nucleotide identity and/or at least 75% amino acid identity. The homology can be calculated using various, publicly available software tools developed by NCBI (Bethesda, Maryland) that can be obtained through the internet (ftp:/ncbi.nlm.nih.gov/pub/). Exemplary tools include the BLAST system available at http://wwww.ncbi.nlm.nih.gov. Pairwise and ClustalW alignments (BLOSUM30 matrix setting) as well as Kyte-Doolittle hydropathic analysis can be obtained using the MacVetor sequence analysis software (Oxford Molecular Group). Watson-Crick complements of the foregoing nucleic acids also are embraced by the invention.

In screening for cancer associated antigen genes, a Southern blot may be performed using the foregoing conditions, together with a radioactive probe. After washing the membrane to which the DNA is finally transferred, the membrane can be placed against X-ray film to detect the radioactive signal. In screening for the expression of cancer associated antigen nucleic acids, Northern blot hybridizations using the foregoing conditions (see also the Examples) can be performed on samples taken from breast cancer patients or subjects suspected of having a condition characterized by expression of breast cancer associated antigen genes. Amplification protocols such as polymerase chain reaction using primers which hybridize to the sequences presented also can be used for detection of the cancer associated antigen genes or expression thereof.

The breast cancer associated genes correspond to SEQ ID NOs. 1-40 and 66. The preferred breast cancer associated antigens for the methods of diagnosis disclosed herein are those set forth in SEQ ID NOs:[31, 33 and 34], which were found to react with allogeneic breast cancer antisera. Encoded polypeptides (e.g., proteins), peptides and antisera thereto are also preferred for diagnosis.

The colon cancer associated genes correspond to SEQ ID Nos. 544-586, even numbers

only. The preferred colon cancer associated antigens for the methods of diagnosis disclosed herein are those, which were found to react with allogeneic colon cancer antisera. Encoded polypeptides (e.g., proteins), peptides and antisera thereto are also preferred for diagnosis.

The preferred gastric cancer associated antigens for the methods of diagnosis disclosed herein are those, which were found to react with allogeneic gastric cancer antisera. Encoded polypeptides (e.g., proteins), peptides and antisera thereto are also preferred for diagnosis.

The gastric cancer associated genes correspond to SEQ ID NOs 176-436 and 588-674.

The renal cancer associated genes correspond to SEQ ID Nos. 89-169, odd numbers only, and 170, 172, and 174. The preferred renal cancer associated antigens for the methods of diagnosis disclosed herein are those, which were found to react with allogeneic renal cancer antisera. Encoded polypeptides (e.g., proteins), peptides and antisera thereto are also preferred for diagnosis.

The lung cancer associated genes correspond to SEQ ID Nos. 689, 691, 692, 694, 696-707, 709, 711, and 712. The preferred lung cancer associated antigens for the methods of diagnosis disclosed herein are those, which were found to react with allogeneic lung cancer antisera. Encoded polypeptides (e.g., proteins), peptides and antisera thereto are also preferred for diagnosis.

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The prostate cancer associated genes correspond to SEQ ID NOs 437-543. The preferred prostate cancer associated antigens for the methods of diagnosis disclosed herein are those, which were found to react with allogeneic prostate cancer antisera. Encoded polypeptides (e.g., proteins), peptides and antisera thereto are also preferred for diagnosis.

The invention also includes degenerate nucleic acids which include alternative codons to those present in the native materials. For example, serine residues are encoded by the codons TCA, AGT, TCC, TCG, TCT and AGC. Each of the six codons is equivalent for the purposes of encoding a serine residue. Thus, it will be apparent to one of ordinary skill in the art that any of the serine-encoding nucleotide triplets may be employed to direct the protein synthesis apparatus, in vitro or in vivo, to incorporate a serine residue into an elongating breast cancer associated antigen polypeptide. Similarly, nucleotide sequence triplets which encode other amino acid residues include, but are not limited to: CCA, CCC, CCG and CCT (proline codons); CGA, CGC, CGG, CGT, AGA and AGG (arginine codons); ACA, ACC, ACG and ACT (threonine codons); AAC and AAT (asparagine codons); and ATA, ATC and ATT (isoleucine codons). Other amino acid residues may be encoded similarly by multiple nucleotide sequences. Thus,

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the invention embraces degenerate nucleic acids that differ from the biologically isolated nucleic acids in codon sequence due to the degeneracy of the genetic code.

The invention also provides isolated unique fragments of cancer associated antigen nucleic acid sequences or complements thereof. A unique fragment is one that is a 'signature' for the larger nucleic acid. It, for example, is long enough to assure that its precise sequence is not found in molecules within the human genome outside of the cancer associated antigen nucleic acids defined above (and human alleles). Those of ordinary skill in the art may apply no more than routine procedures to determine if a fragment is unique within the human genome. Unique fragments, however, exclude fragments completely composed of the nucleotide sequences of any of GenBank accession numbers listed in Table 1 or other previously published sequences as of the filing date of the priority documents for sequences listed in a respective priority document or the filing date of this application for sequences listed for the first time in this application which overlap the sequences of the invention.

A fragment which is completely composed of the sequence described in the foregoing GenBank deposits is one which does not include any of the nucleotides unique to the sequences of the invention. Thus, a unique fragment must contain a nucleotide sequence other than the exact sequence of those in GenBank or fragments thereof. The difference may be an addition, deletion or substitution with respect to the GenBank sequence or it may be a sequence wholly separate from the GenBank sequence.

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Unique fragments can be used as probes in Southern and Northern blot assays to identify such nucleic acids, or can be used in amplification assays such as those employing PCR. As known to those skilled in the art, large probes such as 200, 250, 300 or more nucleotides are preferred for certain uses such as Southern and Northern blots, while smaller fragments will be preferred for uses such as PCR. Unique fragments also can be used to produce fusion proteins for generating antibodies or determining binding of the polypeptide fragments, or for generating immunoassay components. Likewise, unique fragments can be employed to produce nonfused fragments of the cancer associated antigen polypeptides, useful, for example, in the preparation of antibodies, and in immunoassays. Unique fragments further can be used as antisense molecules to inhibit the expression of cancer associated antigen nucleic acids and polypeptides, particularly for therapeutic purposes as described in greater detail below.

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As will be recognized by those skilled in the art, the size of the unique fragment will depend upon its conservancy in the genetic code. Thus, some regions of cancer associated antigen sequences and complements thereof will require longer segments to be unique while others will require only short segments, typically between 12 and 32 nucleotides (e.g. 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, 30, 31 and 32 or more bases long, up to the entire length of the disclosed sequence. As mentioned above, this disclosure intends to embrace each and every fragment of each sequence, beginning at the first nucleotide, the second nucleotide and so on, up to 8 nucleotides short of the end, and ending anywhere from nucleotide number 8, 9, 10 and so on for each sequence, up to the very last nucleotide, (provided the sequence is unique as described above).

Virtually any segment of the polypeptide coding region of novel cancer associated antigen nucleic acids, or complements thereof, that is 18 or more nucleotides in length will be unique. Those skilled in the art are well versed in methods for selecting such sequences, typically on the basis of the ability of the unique fragment to selectively distinguish the sequence of interest from other sequences in the human genome of the fragment to those on known databases typically is all that is necessary, although *in vitro* confirmatory hybridization and sequencing analysis may be performed. Especially preferred include nucleic acids encoding a series of epitopes, known as "polytopes". The epitopes can be arranged in sequential or overlapping fashion (*see, e.g.*, Thomson et al., *Proc. Natl. Acad. Sci. USA* 92:5845-5849, 1995; Gilbert et al., *Nature Biotechnol.* 15:1280-1284, 1997), with or without the natural flanking sequences, and can be separated by unrelated linker sequences if desired. The polytope is processed to generated individual epitopes which are recognized by the immune system for generation of immune responses.

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Thus, for example, peptides derived from a polypeptide having an amino acid sequence encoded by one of the nucleic acid disclosed herein, and which are presented by MHC molecules and recognized by CTL or T helper lymphocytes, can be combined with peptides from one or more other cancer associated antigens (e.g. by preparation of hybrid nucleic acids or polypeptides) to form "polytopes". The two or more peptides (or nucleic acids encoding the peptides) can be selected from those described herein, or they can include one or more peptides of previously known cancer associated antigens. Exemplary cancer associated peptide antigens that can be administered to induce or enhance an immune response are derived from tumor associated genes and encoded proteins including MAGE-1, MAGE-2, MAGE-3, MAGE-4, MAGE-5, MAGE-6, MAGE-7,

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MAGE-8, MAGE-9, MAGE-10, MAGE-11, GAGE-1, GAGE-2, GAGE-3, GAGE-4, GAGE-5, GAGE-6, BAGE-1, RAGE-1, LB33/MUM-1, PRAME, NAG, MAGE-Xp2, MAGE-Xp3, MAGE-Xp4, tyrosinase, brain glycogen phosphorylase, Melan-A, and MAGE-C1. See, for example, PCT application publication no. WO96/10577. Other examples will be known to one of ordinary skill in the art (for example, see Coulie, *Stem Cells* 13:393-403, 1995), and can be used in the invention in a like manner as those disclosed herein. One of ordinary skill in the art can prepare polypeptides comprising one or more peptides and one or more of the foregoing cancer associated peptides, or nucleic acids encoding such polypeptides, according to standard procedures of molecular biology.

Thus polytopes are groups of two or more potentially immunogenic or immune response stimulating peptides which can be joined together in various arrangements (e.g. concatenated, overlapping). The polytope (or nucleic acid encoding the polytope) can be administered in a standard immunization protocol, e.g. to animals, to test the effectiveness of the polytope in stimulating, enhancing and/or provoking an immune response.

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The peptides can be joined together directly or via the use of flanking sequences to form polytopes, and the use of polytopes as vaccines is well known in the art (see, e.g., Thomson et al., *Proc. Acad. Natl. Acad. Sci USA* 92(13):5845-5849, 1995; Gilbert et al., *Nature Biotechnol.* 15(12):1280-1284, 1997; Thomson et al., *J. Immunol.* 157(2):822-826, 1996; Tam et al., *J. Exp. Med.* 171(1):299-306, 1990).for example, Tam showed that polytopes consisting of both MHC class I and class II binding epitopes successfully generated antibody and protective immunity in a mouse model. Tam also demonstrated that polytopes comprising "strings" of epitopes are processed to yield individual epitopes which are presented by MHC molecules and recognized by CTLs. Thus polytopes containing various numbers and combinations of epitopes can be prepared and tested for recognition by CTLs and for efficacy in increasing an immune response.

It is known that tumors express a set of tumor antigens, of which only certain subsets may be expressed in the tumor of any given patient (for examples of this, see the Examples below). Polytopes can be prepared which correspond to the different combination of epitopes representing the subset of tumor rejection antigens expressed in a particular patient. Polytopes also can be prepared to reflect a broader spectrum of tumor rejection antigens known to be expressed by a tumor type. Polytopes can be introduced to a patient in need of such treatment as polypeptide structures, or via the use of nucleic acid delivery systems known in the art (see, e.g., Allsopp et al., Eur. J.

Immunol. 26(8):1951-1959, 1996). Adenovirus, pox virus, Ty-virus like particles, adeno-associated virus, plasmids, bacteria, etc. can be used in such delivery. One can test the polytope delivery systems in mouse models to determine efficacy of the delivery system. The systems also can be tested in human clinical trials.

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In instances in which a human HLA class I molecule presents tumor rejection antigens derived from cancer associated nucleic acids, the expression vector may also include a nucleic acid sequence coding for the HLA molecule that presents any particular tumor rejection antigen derived from these nucleic acids and polypeptides. Alternatively, the nucleic acid sequence coding for such a HLA molecule can be contained within a separate expression vector. In a situation where the vector contains both coding sequences, the single vector can be used to transfect a cell which does not normally express either one. Where the coding sequences for a cancer associated antigen precursor and the HLA molecule which presents it are contained on separate expression vectors, the expression vectors can be cotransfected. The cancer associated antigen precursor coding sequence may be used alone, when, e.g. the host cell already expresses a HLA molecule which presents a cancer associated antigen derived from precursor molecules. Of course, there is no limit on the particular host cell which can be used. As the vectors which contain the two coding sequences may be used in any antigen-presenting cells if desired, and the gene for cancer associated antigen precursor can be used in host cells which do not express a HLA molecule which presents a cancer associated antigen. Further, cell-free transcription systems may be used in lieu of cells.

As mentioned above, the invention embraces antisense oligonucleotides that selectively bind to a nucleic acid molecule encoding a cancer associated antigen polypeptide, to reduce the expression of cancer associated antigens. This is desirable in virtually any medical condition wherein a reduction of expression of cancer associated antigens is desirable, e.g., in the treatment of cancer. This is also useful for *in vitro* or *in vivo* testing of the effects of a reduction of expression of one or more cancer associated antigens.

As used herein, the term "antisense oligonucleotide" or "antisense" describes an oligonucleotide that is an oligoribonucleotide, oligodeoxyribonucleotide, modified oligoribonucleotide, or modified oligodeoxyribonucleotide which hybridizes under physiological conditions to DNA comprising a particular gene or to an mRNA transcript of that gene and, thereby, inhibits the transcription of that gene and/or the translation of that mRNA. The antisense molecules

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are designed so as to interfere with transcription or translation of a target gene upon hybridization with the target gene or transcript. Those skilled in the art will recognize that the exact length of the antisense oligonucleotide and its degree of complementarity with its target will depend upon the specific target selected, including the sequence of the target and the particular bases which comprise that sequence. It is preferred that the antisense oligonucleotide be constructed and arranged so as to bind selectively with the target under physiological conditions, i.e., to hybridize substantially more to the target sequence than to any other sequence in the target cell under physiological conditions. Based upon the sequences of nucleic acids encoding breast cancer associated antigen, or upon allelic or homologous genomic and/or cDNA sequences, one of skill in the art can easily choose and synthesize any of a number of appropriate antisense molecules for use in accordance with the 10 present invention. In order to be sufficiently selective and potent for inhibition, such antisense oligonucleotides should comprise at least 10 and, more preferably, at least 15 consecutive bases which are complementary to the target, although in certain cases modified oligonucleotides as short as 7 bases in length have been used successfully as antisense oligonucleotides (Wagner et al., Nature Biotechnol. 14:840-844, 1996). Most preferably, the antisense oligonucleotides comprise a complementary sequence of 20-30 bases. Although oligonucleotides may be chosen which are antisense to any region of the gene or mRNA transcripts, in preferred embodiments the antisense oligonucleotides correspond to N-terminal or 5' upstream sites such as translation initiation, transcription initiation or promoter sites. In addition, 3'-untranslated regions may be targeted. Targeting to mRNA splicing sites has also been used in the art but may be less preferred if alternative mRNA splicing occurs. In addition, the antisense is targeted, preferably, to sites in which mRNA secondary structure is not expected (see, e.g., Sainio et al., Cell Mol. Neurobiol. 14(5):439-457, 1994) and at which proteins are not expected to bind. Finally, although the listed sequences are cDNA sequences, one of ordinary skill in the art may easily derive the genomic DNA corresponding to the cDNA of a cancer associated antigen. Thus, the present invention also provides for antisense oligonucleotides which are complementary to the genomic DNA corresponding to nucleic acids encoding breast cancer associated antigens. Similarly, antisense to allelic or homologous cDNAs and genomic DNAs are enabled without undue experimentation.

In one set of embodiments, the antisense oligonucleotides of the invention may be composed of "natural" deoxyribonucleotides, ribonucleotides, or any combination thereof. That is, the 5' end

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of one native nucleotide and the 3' end of another native nucleotide may be covalently linked, as in natural systems, via a phosphodiester internucleoside linkage. These oligonucleotides may be prepared by art recognized methods which may be carried out manually or by an automated synthesizer. They also may be produced recombinantly by vectors.

In preferred embodiments, however, the antisense oligonucleotides of the invention also may include "modified" oligonucleotides. That is, the oligonucleotides may be modified in a number of ways which do not prevent them from hybridizing to their target but which enhance their stability or targeting or which otherwise enhance their therapeutic effectiveness.

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The term "modified oligonucleotide" as used herein describes an oligonucleotide in which (1) at least two of its nucleotides are covalently linked via a synthetic internucleoside linkage (i.e., a linkage other than a phosphodiester linkage between the 5' end of one nucleotide and the 3' end of another nucleotide) and/or (2) a chemical group not normally associated with nucleic acids has been covalently attached to the oligonucleotide. Preferred synthetic internucleoside linkages are phosphorothioates, alkylphosphonates, phosphorodithioates, phosphate esters, alkylphosphonothioates, phosphoramidates, carbamates, carbonates, phosphate triesters, acetamidates, carboxymethyl esters and peptides.

The term "modified oligonucleotide" also encompasses oligonucleotides with a covalently modified base and/or sugar. For example, modified oligonucleotides include oligonucleotides having backbone sugars which are covalently attached to low molecular weight organic groups other than a hydroxyl group at the 3' position and other than a phosphate group at the 5' position. Thus modified oligonucleotides may include a 2'-O-alkylated ribose group. In addition, modified oligonucleotides may include sugars such as arabinose instead of ribose. The present invention, thus, contemplates pharmaceutical preparations containing modified antisense molecules that are complementary to and hybridizable with, under physiological conditions, nucleic acids encoding breast cancer associated antigen polypeptides, together with pharmaceutically acceptable carriers.

Antisense oligonucleotides may be administered as part of a pharmaceutical composition. Such a pharmaceutical composition may include the antisense oligonucleotides in combination with any standard physiologically and/or pharmaceutically acceptable carriers which are known in the art. The compositions should be sterile and contain a therapeutically effective amount of the antisense oligonucleotides in a unit of weight or volume suitable for administration to a patient. The term

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"pharmaceutically acceptable" means a non-toxic material that does not interfere with the effectiveness of the biological activity of the active ingredients. The term "physiologically acceptable" refers to a non-toxic material that is compatible with a biological system such as a cell, cell culture, tissue, or organism. The characteristics of the carrier will depend on the route of administration. Physiologically and pharmaceutically acceptable carriers include diluents, fillers, salts, buffers, stabilizers, solubilizers, and other materials which are well known in the art, as further described below.

As used herein, a "vector" may be any of a number of nucleic acids into which a desired sequence may be inserted by restriction and ligation for transport between different genetic 10 environments or for expression in a host cell. Vectors are typically composed of DNA although RNA vectors are also available. Vectors include, but are not limited to, plasmids, phagemids and virus genomes. A cloning vector is one which is able to replicate in a host cell, and which is further characterized by one or more endonuclease restriction sites at which the vector may be cut in a determinable fashion and into which a desired DNA sequence may be ligated such that the new recombinant vector retains its ability to replicate in the host cell. In the case of plasmids, replication of the desired sequence may occur many times as the plasmid increases in copy number within the host bacterium or just a single time per host before the host reproduces by mitosis. In the case of phage, replication may occur actively during a lytic phase or passively during a lysogenic phase. An expression vector is one into which a desired DNA sequence may be inserted by restriction and ligation such that it is operably joined to regulatory sequences and may be expressed as an RNA transcript. Vectors may further contain one or more marker sequences suitable for use in the identification of cells which have or have not been transformed or transfected with the vector. Markers include, for example, genes encoding proteins which increase or decrease either resistance or sensitivity to antibiotics or other compounds, genes which encode enzymes whose activities are detectable by standard assays known in the art (e.g., \( \beta\)-galactosidase or alkaline phosphatase), and genes which visibly affect the phenotype of transformed or transfected cells, hosts, colonies or plaques (e.g., green fluorescent protein). Preferred vectors are those capable of autonomous replication and expression of the structural gene products present in the DNA segments to which they are operably joined.

As used herein, a coding sequence and regulatory sequences are said to be "operably" joined

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when they are covalently linked in such a way as to place the expression or transcription of the coding sequence under the influence or control of the regulatory sequences. If it is desired that the coding sequences be translated into a functional protein, two DNA sequences are said to be operably joined if induction of a promoter in the 5' regulatory sequences results in the transcription of the coding sequence and if the nature of the linkage between the two DNA sequences does not (1) result in the introduction of a frame-shift mutation, (2) interfere with the ability of the promoter region to direct the transcription of the coding sequences, or (3) interfere with the ability of the corresponding RNA transcript to be translated into a protein. Thus, a promoter region would be operably joined to a coding sequence if the promoter region were capable of effecting transcription of that DNA sequence such that the resulting transcript might be translated into the desired protein or polypeptide.

The precise nature of the regulatory sequences needed for gene expression may vary between species or cell types, but shall in general include, as necessary, 5' non-transcribed and 5' non-translated sequences involved with the initiation of transcription and translation respectively, such as a TATA box, capping sequence, CAAT sequence, and the like. Especially, such 5' non-transcribed regulatory sequences will include a promoter region which includes a promoter sequence for transcriptional control of the operably joined gene. Regulatory sequences may also include enhancer sequences or upstream activator sequences as desired. The vectors of the invention may optionally include 5' leader or signal sequences. The choice and design of an appropriate vector is within the ability and discretion of one of ordinary skill in the art.

Expression vectors containing all the necessary elements for expression are commercially available and known to those skilled in the art. See, e.g., Sambrook et al., *Molecular Cloning: A Laboratory Manual*, Second Edition, Cold Spring Harbor Laboratory Press, 1989. Cells are genetically engineered by the introduction into the cells of heterologous DNA (RNA) encoding a breast cancer associated antigen polypeptide or fragment or variant thereof. That heterologous DNA (RNA) is placed under operable control of transcriptional elements to permit the expression of the heterologous DNA in the host cell.

Preferred systems for mRNA expression in mammalian cells are those such as pRc/CMV (available from Invitrogen, Carlsbad, CA) that contain a selectable marker such as a gene that confers G418 resistance (which facilitates the selection of stably transfected cell lines) and the

human cytomegalovirus (CMV) enhancer-promoter sequences. Additionally, suitable for expression in primate or canine cell lines is the pCEP4 vector (Invitrogen), which contains an Epstein Barr Virus (EBV) origin of replication, facilitating the maintenance of plasmid as a multicopy extrachromosomal element. Another expression vector is the pEF-BOS plasmid containing the promoter of polypeptide Elongation Factor 1α, which stimulates efficiently transcription *in vitro*. The plasmid is described by Mishizuma and Nagata (*Nuc. Acids Res.* 18:5322, 1990), and its use in transfection experiments is disclosed by, for example, Demoulin (*Mol. Cell. Biol.* 16:4710-4716, 1996). Still another preferred expression vector is an adenovirus, described by Stratford-Perricaudet, which is defective for E1 and E3 proteins (*J. Clin. Invest.* 90:626-630, 1992). The use of the adenovirus as an Adeno.P1A recombinant for the expression of an antigen is disclosed by Warnier et al., in intradermal injection in mice for immunization against P1A (*Int. J. Cancer*, 67:303-310, 1996). Additional vectors for delivery of nucleic acid are provided below.

The invention also embraces so-called expression kits, which allow the artisan to prepare a desired expression vector or vectors. Such expression kits include at least separate portions of a vector and one or more of the previously discussed breast cancer associated antigen nucleic acid molecules. Other components may be added, as desired, as long as the previously mentioned nucleic acid molecules, which are required, are included. The invention also includes kits for amplification of a breast cancer associated antigen nucleic acid, including at least one pair of amplification primers which hybridize to a breast cancer associated antigen nucleic acid. The primers preferably are 12-32 nucleotides in length and are non-overlapping to prevent formation of "primer-dimers". One of the primers will hybridize to one strand of the breast cancer associated antigen nucleic acid and the second primer will hybridize to the complementary strand of the breast cancer associated antigen nucleic acid, in an arrangement which permits amplification of the breast cancer associated antigen nucleic acid. Selection of appropriate primer pairs is standard in the art. For example, the selection can be made with assistance of a computer program designed for such a purpose, optionally followed by testing the primers for amplification specificity and efficiency.

The invention also permits the construction of cancer associated antigen gene "knock-outs" in cells and in animals, providing materials for studying certain aspects of cancer and immune system responses to cancer.

The invention also provides isolated polypeptides (including whole proteins and partial

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proteins) encoded by the foregoing cancer associated antigen nucleic acids. Such polypeptides are useful, for example, alone or as fusion proteins to generate antibodies, as components of an immunoassay or diagnostic assay or as therapeutics. Cancer associated antigen polypeptides can be isolated from biological samples including tissue or cell homogenates, and can also be expressed recombinantly in a variety of prokaryotic and eukaryotic expression systems by constructing an expression vector appropriate to the expression system, introducing the expression vector into the expression system, and isolating the recombinantly expressed protein. Short polypeptides, including antigenic peptides (such as are presented by MHC molecules on the surface of a cell for immune recognition) also can be synthesized chemically using well-established methods of peptide synthesis.

A unique fragment of a cancer associated antigen polypeptide, in general, has the features and characteristics of unique fragments as discussed above in connection with nucleic acids. As will be recognized by those skilled in the art, the size of the unique fragment will depend upon factors such as whether the fragment constitutes a portion of a conserved protein domain. Thus, some regions of breast cancer associated antigens will require longer segments to be unique while others will require only short segments, typically between 5 and 12 amino acids (e.g. 5, 6, 7, 8, 9, 10, 11 or 12 or more, including each integer up to the full length, amino acids long).

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Unique fragments of a polypeptide preferably are those fragments which retain a distinct functional capability of the polypeptide. Functional capabilities which can be retained in a unique fragment of a polypeptide include interaction with antibodies, interaction with other polypeptides or fragments thereof, selective binding of nucleic acids or proteins, and enzymatic activity. One important activity is the ability to act as a signature for identifying the polypeptide. Another is the ability to complex with HLA and to provoke in a human an immune response. Those skilled in the art are well versed in methods for selecting unique amino acid sequences, typically on the basis of the ability of the unique fragment to selectively distinguish the sequence of interest from non-family members. A comparison of the sequence of the fragment to those on known databases typically is all that is necessary.

The invention embraces variants of the cancer associated antigen polypeptides described above. As used herein, a "variant" of a cancer associated antigen polypeptide is a polypeptide which contains one or more modifications to the primary amino acid sequence of a cancer associated antigen polypeptide. Modifications which create a cancer associated antigen variant can be made to

a cancer associated antigen polypeptide 1) to reduce or eliminate an activity of a cancer associated antigen polypeptide; 2) to enhance a property of a cancer associated antigen polypeptide, such as protein stability in an expression system or the stability of protein-protein binding; 3) to provide a novel activity or property to a cancer associated antigen polypeptide, such as addition of an antigenic epitope or addition of a detectable moiety; or 4) to provide equivalent or better binding to an HLA molecule. Modifications to a cancer associated antigen polypeptide are typically made to the nucleic acid which encodes the cancer associated antigen polypeptide, and can include deletions, point mutations, truncations, amino acid substitutions and additions of amino acids or non-amino acid mojeties. Alternatively, modifications can be made directly to the polypeptide, such as by cleavage, addition of a linker molecule, addition of a detectable moiety, such as biotin, addition of a fatty acid, and the like. Modifications also embrace fusion proteins comprising all or part of the cancer associated antigen amino acid sequence. One of skill in the art will be familiar with methods for predicting the effect on protein conformation of a change in protein sequence, and can thus "design" a variant cancer associated antigen polypeptide according to known methods. One example of such a method is described by Dahiyat and Mayo in Science 278:82-87, 1997, whereby proteins can be designed de novo. The method can be applied to a known protein to vary a only a portion of the polypeptide sequence. By applying the computational methods of Dahiyat and Mayo, specific variants of a cancer associated antigen polypeptide can be proposed and tested to determine whether the variant retains a desired conformation.

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In general, variants include cancer associated antigen polypeptides which are modified specifically to alter a feature of the polypeptide unrelated to its desired physiological activity. For example, cysteine residues can be substituted or deleted to prevent unwanted disulfide linkages. Similarly, certain amino acids can be changed to enhance expression of a breast cancer associated antigen polypeptide by eliminating proteolysis by proteases in an expression system (e.g., dibasic amino acid residues in yeast expression systems in which KEX2 protease activity is present).

Mutations of a nucleic acid which encode a cancer associated antigen polypeptide preferably preserve the amino acid reading frame of the coding sequence, and preferably do not create regions in the nucleic acid which are likely to hybridize to form secondary structures, such a hairpins or loops, which can be deleterious to expression of the variant polypeptide.

Mutations can be made by selecting an amino acid substitution, or by random mutagenesis of

a selected site in a nucleic acid which encodes the polypeptide. Variant polypeptides are then expressed and tested for one or more activities to determine which mutation provides a variant polypeptide with the desired properties. Further mutations can be made to variants (or to non-variant cancer associated antigen polypeptides) which are silent as to the amino acid sequence of the polypeptide, but which provide preferred codons for translation in a particular host. The preferred codons for translation of a nucleic acid in, e.g., *E. coli*, are well known to those of ordinary skill in the art. Still other mutations can be made to the noncoding sequences of a cancer associated antigen gene or cDNA clone to enhance expression of the polypeptide. The activity of variants of cancer associated antigen polypeptides can be tested by cloning the gene encoding the variant cancer associated antigen polypeptide into a bacterial or mammalian expression vector, introducing the vector into an appropriate host cell, expressing the variant cancer associated antigen polypeptide, and testing for a functional capability of the cancer associated antigen polypeptides as disclosed herein. For example, the variant cancer associated antigen polypeptide can be tested for reaction with autologous or allogeneic sera as disclosed in the Examples. Preparation of other variant polypeptides may favor testing of other activities, as will be known to one of ordinary skill in the art.

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The skilled artisan will also realize that conservative amino acid substitutions may be made in cancer associated antigen polypeptides to provide functionally equivalent variants of the foregoing polypeptides, i.e, the variants retain the functional capabilities of the cancer associated antigen polypeptides. As used herein, a "conservative amino acid substitution" refers to an amino acid substitution which does not alter the relative charge or size characteristics of the protein in which the amino acid substitution is made. Variants can be prepared according to methods for altering polypeptide sequence known to one of ordinary skill in the art such as are found in references which compile such methods, e.g. *Molecular Cloning: A Laboratory Manual*, J. Sambrook, et al., eds., Second Edition, Cold Spring Harbor Laboratory Press, Cold Spring Harbor, New York, 1989, or *Current Protocols in Molecular Biology*, F.M. Ausubel, et al., eds., John Wiley & Sons, Inc., New York. Exemplary functionally equivalent variants of the cancer associated antigen polypeptides include conservative amino acid substitutions of in the amino acid sequences of SEQ ID proteins disclosed herein. Conservative substitutions of amino acids include substitutions made amongst amino acids within the following groups: (a) M, I, L, V; (b) F, Y, W; (c) K, R, H; (d) A, G; (e) S, T; (f) Q, N; and (g) E, D.

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For example, upon determining that a peptide derived from a cancer associated antigen polypeptide is presented by an MHC molecule and recognized by CTLs (e.g., as described in the Examples), one can make conservative amino acid substitutions to the amino acid sequence of the peptide, particularly at residues which are thought not to be direct contact points with the MHC molecule. For example, methods for identifying functional variants of HLA class II binding peptides are provided in a published PCT application of Strominger and Wucherpfennig (PCT/US96/03182). Peptides bearing one or more amino acid substitutions also can be tested for concordance with known HLA/MHC motifs prior to synthesis using, e.g. the computer program described by D'Amaro and Drijfhout (D'Amaro et al., *Human Immunol.* 43:13-18, 1995; Drijfhout et al., *Human Immunol.* 43:1-12, 1995). The substituted peptides can then be tested for binding to the MHC molecule and recognition by CTLs when bound to MHC. These variants can be tested for improved stability and are useful, *inter alia*, in vaccine compositions.

Conservative amino-acid substitutions in the amino acid sequence of cancer associated antigen polypeptides to produce functionally equivalent variants of cancer associated antigen polypeptides typically are made by alteration of a nucleic acid encoding a cancer associated antigen polypeptide. Such substitutions can be made by a variety of methods known to one of ordinary skill in the art. For example, amino acid substitutions may be made by PCR-directed mutation, sitedirected mutagenesis according to the method of Kunkel (Kunkel, Proc. Nat. Acad. Sci. U.S.A. 82: 488-492, 1985), or by chemical synthesis of a gene encoding a cancer associated antigen polypeptide. Where amino acid substitutions are made to a small unique fragment of a cancer associated antigen polypeptide, such as an antigenic epitope recognized by autologous or allogeneic sera or cytolytic T lymphocytes, the substitutions can be made by directly synthesizing the peptide. The activity of functionally equivalent fragments of cancer associated antigen polypeptides can be tested by cloning the gene encoding the altered cancer associated antigen polypeptide into a bacterial or mammalian expression vector, introducing the vector into an appropriate host cell, expressing the altered cancer associated antigen polypeptide, and testing for a functional capability of the cancer associated antigen polypeptides as disclosed herein. Peptides which are chemically synthesized can be tested directly for function, e.g., for binding to antisera recognizing associated antigens.

The invention as described herein has a number of uses, some of which are described elsewhere herein. First, the invention permits isolation of the cancer associated antigen protein

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molecules. A variety of methodologies well-known to the skilled practitioner can be utilized to obtain isolated cancer associated antigen molecules. The polypeptide may be purified from cells which naturally produce the polypeptide by chromatographic means or immunological recognition. Alternatively, an expression vector may be introduced into cells to cause production of the polypeptide. In another method, mRNA transcripts may be microinjected or otherwise introduced into cells to cause production of the encoded polypeptide. Translation of mRNA in cell-free extracts such as the reticulocyte lysate system also may be used to produce polypeptide. Those skilled in the art also can readily follow known methods for isolating cancer associated antigen polypeptides. These include, but are not limited to, immunochromatography, HPLC, size-exclusion chromatography, ion-exchange chromatography and immune-affinity chromatography.

The isolation and identification of cancer associated antigen genes also makes it possible for the artisan to diagnose a disorder characterized by expression of cancer associated antigens. These methods involve determining expression of one or more cancer associated antigen nucleic acids, and/or encoded cancer associated antigen polypeptides and/or peptides derived therefrom. In the former situation, such determinations can be carried out via any standard nucleic acid determination assay, including the polymerase chain reaction, or assaying with labeled hybridization probes. In the latter situation, such determinations can be carried out by screening patient antisera for recognition of the polypeptide.

The invention also makes it possible isolate proteins which bind to cancer associated antigens as disclosed herein, including antibodies and cellular binding partners of the cancer associated antigens. Additional uses are described further herein.

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The invention also provides, in certain embodiments, "dominant negative" polypeptides derived from cancer associated antigen polypeptides. A dominant negative polypeptide is an inactive variant of a protein, which, by interacting with the cellular machinery, displaces an active protein from its interaction with the cellular machinery or competes with the active protein, thereby reducing the effect of the active protein. For example, a dominant negative receptor which binds a ligand but does not transmit a signal in response to binding of the ligand can reduce the biological effect of expression of the ligand. Likewise, a dominant negative catalytically-inactive kinase which interacts normally with target proteins but does not phosphorylate the target proteins can reduce phosphorylation of the target proteins in response to a cellular signal. Similarly, a dominant

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negative transcription factor which binds to a promoter site in the control region of a gene but does not increase gene transcription can reduce the effect of a normal transcription factor by occupying promoter binding sites without increasing transcription.

The end result of the expression of a dominant negative polypeptide in a cell is a reduction in function of active proteins. One of ordinary skill in the art can assess the potential for a dominant negative variant of a protein, and using standard mutagenesis techniques to create one or more dominant negative variant polypeptides. For example, given the teachings contained herein of cancer associated antigens, especially those which are similar to known proteins which have known activities, one of ordinary skill in the art can modify the sequence of the cancer associated antigens by site-specific mutagenesis, scanning mutagenesis, partial gene deletion or truncation, and the like. See, e.g., U.S. Patent No. 5,580,723 and Sambrook et al., *Molecular Cloning: A Laboratory Manual*, Second Edition, Cold Spring Harbor Laboratory Press, 1989. The skilled artisan then can test the population of mutagenized polypeptides for diminution in a selected and/or for retention of such an activity. Other similar methods for creating and testing dominant negative variants of a protein will be apparent to one of ordinary skill in the art.

The invention also involves agents such as polypeptides which bind to cancer associated antigen polypeptides. Such binding agents can be used, for example, in screening assays to detect the presence or absence of cancer associated antigen polypeptides and complexes of cancer associated antigen polypeptides and their binding partners and in purification protocols to isolated cancer associated antigen polypeptides and complexes of cancer associated antigen polypeptides and their binding partners. Such agents also can be used to inhibit the native activity of the cancer associated antigen polypeptides, for example, by binding to such polypeptides.

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The invention, therefore, embraces peptide binding agents which, for example, can be antibodies or fragments of antibodies having the ability to selectively bind to cancer associated antigen polypeptides. Antibodies include polyclonal and monoclonal antibodies, prepared according to conventional methodology.

Significantly, as is well-known in the art, only a small portion of an antibody molecule, the paratope, is involved in the binding of the antibody to its epitope (see, in general, Clark, W.R. (1986) The Experimental Foundations of Modern Immunology Wiley & Sons, Inc., New York; Roitt, I. (1991) Essential Immunology, 7th Ed., Blackwell Scientific Publications, Oxford). The

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pFc' and Fc regions, for example, are effectors of the complement cascade but are not involved in antigen binding. An antibody from which the pFc' region has been enzymatically cleaved, or which has been produced without the pFc' region, designated an F(ab')<sub>2</sub> fragment, retains both of the antigen binding sites of an intact antibody. Similarly, an antibody from which the Fc region has been enzymatically cleaved, or which has been produced without the Fc region, designated an Fab fragment, retains one of the antigen binding sites of an intact antibody molecule. Proceeding further, Fab fragments consist of a covalently bound antibody light chain and a portion of the antibody heavy chain denoted Fd. The Fd fragments are the major determinant of antibody specificity (a single Fd fragment may be associated with up to ten different light chains without altering antibody specificity) and Fd fragments retain epitope-binding ability in isolation.

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Within the antigen-binding portion of an antibody, as is well-known in the art, there are complementarity determining regions (CDRs), which directly interact with the epitope of the antigen, and framework regions (FRs), which maintain the tertiary structure of the paratope (see, in general, Clark, 1986; Roitt, 1991). In both the heavy chain Fd fragment and the light chain of IgG immunoglobulins, there are four framework regions (FR1 through FR4) separated respectively by three complementarity determining regions (CDR1 through CDR3). The CDRs, and in particular the CDR3 regions, and more particularly the heavy chain CDR3, are largely responsible for antibody specificity.

It is now well-established in the art that the non-CDR regions of a mammalian antibody may be replaced with similar regions of conspecific or heterospecific antibodies while retaining the epitopic specificity of the original antibody. This is most clearly manifested in the development and use of "humanized" antibodies in which non-human CDRs are covalently joined to human FR and/or Fc/pFc' regions to produce a functional antibody. Thus, for example, PCT International Publication Number WO 92/04381 teaches the production and use of humanized murine RSV antibodies in which at least a portion of the murine FR regions have been replaced by FR regions of human origin. Such antibodies, including fragments of intact antibodies with antigen-binding ability, are often referred to as "chimeric" antibodies.

Thus, as will be apparent to one of ordinary skill in the art, the present invention also provides for F(ab')<sub>2</sub>, Fab, Fv and Fd fragments; chimeric antibodies in which the Fc and/or FR and/or CDR1 and/or CDR2 and/or light chain CDR3 regions have been replaced by homologous

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human or non-human sequences; chimeric F(ab')<sub>2</sub> fragment antibodies in which the FR and/or CDR1 and/or CDR2 and/or light chain CDR3 regions have been replaced by homologous human or non-human sequences; chimeric Fab fragment antibodies in which the FR and/or CDR1 and/or CDR2 and/or light chain CDR3 regions have been replaced by homologous human or non-human sequences; and chimeric Fd fragment antibodies in which the FR and/or CDR1 and/or CDR2 regions have been replaced by homologous human or non-human sequences. The present invention also includes so-called single chain antibodies.

Thus, the invention involves polypeptides of numerous size and type that bind specifically to cancer associated antigen polypeptides, and complexes of both cancer associated antigen polypeptides and their binding partners. These polypeptides may be derived also from sources other than antibody technology. For example, such polypeptide binding agents can be provided by degenerate peptide libraries which can be readily prepared in solution, in immobilized form or as phage display libraries. Combinatorial libraries also can be synthesized of peptides containing one or more amino acids. Libraries further can be synthesized of peptoids and non-peptide synthetic moieties.

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Phage display can be particularly effective in identifying binding peptides useful according to the invention. Briefly, one prepares a phage library (using e.g. m13, fd, or lambda phage), displaying inserts from 4 to about 80 amino acid residues using conventional procedures. The inserts may represent, for example, a completely degenerate or biased array. One then can select phage-bearing inserts which bind to the cancer associated antigen polypeptide. This process can be repeated through several cycles of reselection of phage that bind to the cancer associated antigen polypeptide. Repeated rounds lead to enrichment of phage bearing particular sequences. DNA sequence analysis can be conducted to identify the sequences of the expressed polypeptides. The minimal linear portion of the sequence that binds to the cancer associated antigen polypeptide can be determined. One can repeat the procedure using a biased library containing inserts containing part or all of the minimal linear portion plus one or more additional degenerate residues upstream or downstream thereof. Yeast two-hybrid screening methods also may be used to identify polypeptides that bind to the cancer associated antigen polypeptides. Thus, the cancer associated antigen polypeptides of the invention, or a fragment thereof, can be used to screen peptide libraries, including phage display libraries, to identify and select peptide binding partners of the cancer

associated antigen polypeptides of the invention. Such molecules can be used, as described, for screening assays, for purification protocols, for interfering directly with the functioning of cancer associated antigen and for other purposes that will be apparent to those of ordinary skill in the art.

As detailed herein, the foregoing antibodies and other binding molecules may be used for example to identify tissues expressing protein or to purify protein. Antibodies also may be coupled to specific diagnostic labeling agents for imaging of cells and tissues that express cancer associated antigens or to therapeutically useful agents according to standard coupling procedures. Diagnostic agents include, but are not limited to, barium sulfate, iocetamic acid, iopanoic acid, ipodate calcium, diatrizoate sodium, diatrizoate meglumine, metrizamide, tyropanoate sodium and radiodiagnostics including positron emitters such as fluorine-18 and carbon-11, gamma emitters such as iodine-123, technitium-99m, iodine-131 and indium-111, nuclides for nuclear magnetic resonance such as fluorine and gadolinium. Other diagnostic agents useful in the invention will be apparent to one of ordinary skill in the art. As used herein, "therapeutically useful agents" include any therapeutic molecule which desirably is targeted selectively to a cell expressing one of the cancer antigens disclosed herein, including antineoplastic agents, radioiodinated compounds, toxins, other cytostatic or cytolytic drugs, and so forth. Antineoplastic therapeutics are well known and include: aminoglutethimide, azathioprine, bleomycin sulfate, busulfan, carmustine, chlorambucil, cisplatin, cyclophosphamide, cyclosporine, cytarabidine, dacarbazine, dactinomycin, daunorubicin. doxorubicin, taxol, etoposide, fluorouracil, interferon-α, lomustine, mercaptopurine, methotrexate, mitotane, procarbazine HCl, thioguanine, vinblastine sulfate and vincristine sulfate. Additional antineoplastic agents include those disclosed in Chapter 52, Antineoplastic Agents (Paul Calabresi and Bruce A. Chabner), and the introduction thereto, 1202-1263, of Goodman and Gilman's "The Pharmacological Basis of Therapeutics", Eighth Edition, 1990, McGraw-Hill, Inc. (Health Professions Division). Toxins can be proteins such as, for example, pokeweed anti-viral protein, cholera toxin, pertussis toxin, ricin, gelonin, abrin, diphtheria exotoxin, or Pseudomonas exotoxin. Toxin moieties can also be high energy-emitting radionuclides such as cobalt-60.

In the foregoing methods, antibodies prepared according to the invention also preferably are specific for the cancer associated antigen/MHC complexes described herein.

When "disorder" is used herein, it refers to any pathological condition where the cancer associated antigens are expressed. An example of such a disorder is cancer, breast, colon, gastric,

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renal, prostate and lung cancers as particular examples.

Samples of tissue and/or cells for use in the various methods described herein can be obtained through standard methods such as tissue biopsy, including punch biopsy and cell scraping, and collection of blood or other bodily fluids by aspiration or other methods.

In certain embodiments of the invention, an immunoreactive cell sample is removed from a subject. By "immunoreactive cell" is meant a cell which can mature into an immune cell (such as a B cell, a helper T cell, or a cytolytic T cell) upon appropriate stimulation. Thus immunoreactive cells include CD34\* hematopoietic stem cells, immature T cells and immature B cells. When it is desired to produce cytolytic T cells which recognize a cancer associated antigen, the immunoreactive cell is contacted with a cell which expresses a cancer associated antigen under conditions favoring production, differentiation and/or selection of cytolytic T cells; the differentiation of the T cell precursor into a cytolytic T cell upon exposure to antigen is similar to clonal selection of the immune system.

Some therapeutic approaches based upon the disclosure are premised on a response by a subject's immune system, leading to lysis of antigen presenting cells, such as breast cancer cells which present one or more cancer associated antigens. One such approach is the administration of autologous CTLs specific to a cancer associated antigen/MHC complex to a subject with abnormal cells of the phenotype at issue. It is within the ability of one of ordinary skill in the art to develop such CTLs in vitro. An example of a method for T cell differentiation is presented in International Application number PCT/US96/05607. Generally, a sample of cells taken from a subject, such as blood cells, are contacted with a cell presenting the complex and capable of provoking CTLs to proliferate. The target cell can be a transfectant, such as a COS cell of the type described herein. These transfectants present the desired complex of their surface and, when combined with a CTL of interest, stimulate its proliferation. COS cells, such as those used herein are widely available, as are other suitable host cells. Specific production of a CTL clone is described herein, and is well known in the art. The clonally expanded autologous CTLs then are administered to the subject.

Another method for selecting antigen-specific CTL clones has recently been described (Altman et al., Science 274:94-96, 1996; Dunbar et al., Curr. Biol. 8:413-416, 1998), in which fluorogenic tetramers of MHC class I molecule/peptide complexes are used to detect specific CTL clones. Briefly, soluble MHC class I molecules are folded in vitro in the presence of β<sub>2</sub>-

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microglobulin and a peptide antigen which binds the class I molecule. After purification, the MHC/peptide complex is purified and labeled with biotin. Tetramers are formed by mixing the biotinylated peptide-MHC complex with labeled avidin (e.g. phycoerythrin) at a molar ratio or 4:1. Tetramers are then contacted with a source of CTLs such as peripheral blood or lymph node. The tetramers bind CTLs which recognize the peptide antigen/MHC class I complex. Cells bound by the tetramers can be sorted by fluorescence activated cell sorting to isolate the reactive CTLs. The isolated CTLs then can be expanded *in vitro* for use as described herein.

To detail a therapeutic methodology, referred to as adoptive transfer (Greenberg, *J. Immunol*. 136(5): 1917, 1986; Riddel et al., *Science* 257: 238, 1992; Lynch et al, *Eur. J. Immunol*. 21: 1403-1410,1991; Kast et al., *Cell* 59: 603-614, 1989), cells presenting the desired complex are combined with CTLs leading to proliferation of the CTLs specific thereto. The proliferated CTLs are then administered to a subject with a cellular abnormality which is characterized by certain of the abnormal cells presenting the particular complex. The CTLs then lyse the abnormal cells, thereby achieving the desired therapeutic goal.

The foregoing therapy assumes that at least some of the subject's abnormal cells present the relevant HLA cancer associated antigen complex. This can be determined very easily, as the art is very familiar with methods for identifying cells which present a particular HLA molecule, as well as how to identify cells expressing DNA of the pertinent sequences, in this case a cancer associated antigen sequence. Once cells presenting the relevant complex are identified via the foregoing screening methodology, they can be combined with a sample from a patient, where the sample contains CTLs. If the complex presenting cells are lysed by the mixed CTL sample, then it can be assumed that a cancer associated antigen is being presented, and the subject is an appropriate candidate for the therapeutic approaches set forth *supra*.

Adoptive transfer is not the only form of therapy that is available in accordance with the invention. CTLs can also be provoked *in vivo*, using a number of approaches. One approach is the use of non-proliferative cells expressing the complex. The cells used in this approach may be those that normally express the complex, such as irradiated tumor cells or cells transfected with one or both of the genes necessary for presentation of the complex (i.e. the antigenic peptide and the presenting HLA molecule). Chen et al. (*Proc. Natl. Acad. Sci. USA* 88: 110-114,1991) exemplifies this approach, showing the use of transfected cells expressing HPVE7 peptides in a therapeutic

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regime. Various cell types may be used. Similarly, vectors carrying one or both of the genes of interest may be used. Viral or bacterial vectors are especially preferred. For example, nucleic acids which encode a breast cancer associated antigen polypeptide or peptide may be operably linked to promoter and enhancer sequences which direct expression of the cancer associated antigen polypeptide or peptide in certain tissues or cell types. The nucleic acid may be incorporated into an expression vector. Expression vectors may be unmodified extrachromosomal nucleic acids, plasmids or viral genomes constructed or modified to enable insertion of exogenous nucleic acids, such as those encoding cancer associated antigen, as described elsewhere herein. Nucleic acids encoding a cancer associated antigen also may be inserted into a retroviral genome, thereby facilitating integration of the nucleic acid into the genome of the target tissue or cell type. In these systems, the gene of interest is carried by a microorganism, e.g., a Vaccinia virus, retrovirus or adenovirus, and the materials de facto "infect" host cells. The cells which result present the complex of interest, and are recognized by autologous CTLs, which then proliferate.

A similar effect can be achieved by combining the cancer associated antigen or a stimulatory fragment thereof with an adjuvant to facilitate incorporation into antigen presenting cells *in vivo*. The breast cancer associated antigen polypeptide is processed to yield the peptide partner of the HLA molecule while a cancer associated antigen peptide may be presented without the need for further processing. Generally, subjects can receive an intradermal injection of an effective amount of the cancer associated antigen. Initial doses can be followed by booster doses, following immunization protocols standard in the art. Preferred cancer associated antigens include those found to react with allogeneic cancer antisera, such as the nucleic acids (and encoded polypeptides and peptides) of SEQ ID NO:31,33 and 34 and others, for example, shown in the examples below.

The invention involves the use of various materials disclosed herein to "immunize" subjects or as "vaccines". As used herein, "immunization" or "vaccination" means increasing or activating an immune response against an antigen. It does not require elimination or eradication of a condition but rather contemplates the clinically favorable enhancement of an immune response toward an antigen. Generally accepted animal models can be used for testing of immunization against breast cancer using a cancer associated antigen nucleic acid. For example, cancer cells can be introduced into a mouse to create a tumor, and one or more cancer associated antigen nucleic acids can be delivered by the methods described herein. The effect on the cancer cells (e.g., reduction of tumor

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size) can be assessed as a measure of the effectiveness of the cancer associated antigen nucleic acid immunization. Of course, testing of the foregoing animal model using more conventional methods for immunization include the administration of one or more cancer associated antigen polypeptides or peptides derived therefrom, optionally combined with one or more adjuvants and/or cytokines to boost the immune response. Methods for immunization, including formulation of a vaccine composition and selection of doses, route of administration and the schedule of administration (e.g. primary and one or more booster doses), are well known in the art. The tests also can be performed in humans, where the end point is to test for the presence of enhanced levels of circulating CTLs against cells bearing the antigen, to test for levels of circulating antibodies against the antigen, to test for the presence of cells expressing the antigen and so forth.

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As part of the immunization compositions, one or more cancer associated antigens or stimulatory fragments thereof are administered with one or more adjuvants to induce an immune response or to increase an immune response. An adjuvant is a substance incorporated into or administered with antigen which potentiates the immune response. Adjuvants may enhance the immunological response by providing a reservoir of antigen (extracellularly or within macrophages), activating macrophages and stimulating specific sets of lymphocytes. Adjuvants of many kinds are well known in the art. Specific examples of adjuvants include monophosphoryl lipid A (MPL, SmithKline Beecham), a congener obtained after purification and acid hydrolysis of Salmonella minnesota Re 595 lipopolysaccharide; saponins including QS21 (SmithKline Beecham), a pure OA-21 saponin purified from *Quillja saponaria* extract; DQS21, described in PCT application WO96/33739 (SmithKline Beecham); QS-7, QS-17, QS-18, and QS-L1 (So et al., Mol. Cells 7:178-186, 1997); incomplete Freund's adjuvant; complete Freund's adjuvant; montanide; and various water-in-oil emulsions prepared from biodegradable oils such as squalene and/or tocopherol. Preferably, the peptides are administered mixed with a combination of DQS21/MPL. The ratio of DOS21 to MPL typically will be about 1:10 to 10:1, preferably about 1:5 to 5:1 and more preferably about 1:1. Typically for human administration, DQS21 and MPL will be present in a vaccine formulation in the range of about 1 µg to about 100 µg. Other adjuvants are known in the art and can be used in the invention (see, e.g. Goding, Monoclonal Antibodies: Principles and Practice, 2nd Ed., 1986). Methods for the preparation of mixtures or emulsions of peptide and adjuvant are well known to those of skill in the art of vaccination.

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Other agents which stimulate the immune response of the subject can also be administered to the subject. For example, other cytokines are also useful in vaccination protocols as a result of their lymphocyte regulatory properties. Many other cytokines useful for such purposes will be known to one of ordinary skill in the art, including interleukin-12 (IL-12) which has been shown to enhance the protective effects of vaccines (see, e.g., Science 268: 1432-1434, 1995), GM-CSF and IL-18. Thus cytokines can be administered in conjunction with antigens and adjuvants to increase the immune response to the antigens.

There are a number of immune response potentiating compounds that can be used in vaccination protocols. These include costimulatory molecules provided in either protein or nucleic acid form. Such costimulatory molecules include the B7-1 and B7-2 (CD80 and CD86 respectively) molecules which are expressed on dendritic cells (DC) and interact with the CD28 molecule expressed on the T cell. This interaction provides costimulation (signal 2) to an antigen/MHC/TCR stimulated (signal 1) T cell, increasing T cell proliferation and effector function. B7 also interacts with CTLA4 (CD152) on T cells and studies involving CTLA4 and B7 ligands indicate that the B7-CTLA4 interaction can enhance antitumor immunity and CTL proliferation, Zheng P., et al. PNAS 95 (11) 6284-6289 (1998).

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B7 typically is not expressed on tumor cells so they are not efficient antigen presenting cells (APCs) for T cells. Induction of B7 expression would enable the tumor cells to stimulate more efficiently CTL proliferation and effector function. A combination of B7/IL-6/IL-12 costimulation has been shown to induce IFN-gamma and a Th1 cytokine profile in the T cell population leading to further enhanced T cell activity, Gajewski et al., J. I mmunol, 154:5637-5648 (1995). Tumor cell transfection with B7 has ben discussed in relation to in vitro CTL expansion for adoptive transfer immunotherapy by Wang et al., J Immunol, 19:1-8 (1986). Other delivery mechanisms for the B7 molecule would include nucleic acid (naked DNA) immunization Kim J., et al. Nat Biotechnol., 15:7:641-646 (1997) and recombinant viruses such as adeno and pox (Wendtner et al., Gene Ther, 4:7:726-735 (1997)). These systems are all amenable to the construction and use of expression cassettes for the coexpression of B7 with other molecules of choice such as the antigens or fragment(s) of antigens discussed herein (including polytopes) or cytokines. These delivery systems can be used for induction of the appropriate molecules in vitro and for in vivo vaccination situations.

The use of anti-CD28 antibodies to directly stimulate T cells in vitro and in vivo could also be

considered.

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Lymphocyte function associated antigen-3 (LFA-3) is expressed on APCs and some tumor cells and interacts with CD2 expressed on T cells. This interaction induces T cell IL-2 and IFN-gamma production and can thus complement but not substitute, the B7/CD28 costimulatory interaction, Parra et al., *J. Immunol.*, 158:637-642 (1997), Fenton et al., *J. Immunother*, 21:2:95-108 (1989).

Lymphocyte function associated antigen-1 (LFA-1) is expressed on leukocytes and interacts with ICAM-1 expressed on APCs and some tumor cells. This interaction induces T cell IL-2 and IFN-gamma production and can thus complement but not substitute, the B7/CD28 costimulatory interaction, Fenton et al., *J. Immunothera*, 21:2:95-108 (1998). LFA-1 is thus a further example of a costimulatory molecule that could be provided in a vaccination protocol in the various ways discussed above for B7.

Complete CTL activation and effector function requires Th cell help through the interaction between the Th cell CD40L (CD40 ligand) molecule and the CD40 molecule expressed by DCS, Ridge et al., *Nature*, 393:474 (1998), Bennett et al., *Nature*, 393:478 (1998), Schoenberger et al., *Nature*, 393:480 (1998). This mechanism of this costimulatory signal is likely to involve upregulation of B7 and associated IL-6/IL-12 production by the DC (APC). The CD40-CD40L interaction thus complements the signal 1 (antigen/MHC-TCR) and signal 2 (B7-CD28) interactions.

The use of anti-CD40 antibodies to stimulate DC cells directly, would be expected to enhance a response to tumor antigens which are normally encountered outside of a inflammatory context or are presented by non-professional APCs (tumor cells). In these situations Th help and B7 costimulation signals are not provided. This mechanism might be used in the context of antigen pulsed DC based therapies or in situations where Th epitopes have not been defined within known TRA precursors.

A cancer associated antigen polypeptide, or a fragment thereof, also can be used to isolate their native binding partners. Isolation of such binding partners may be performed according to well-known methods. For example, isolated cancer associated antigen polypeptides can be attached to a substrate (e.g., chromatographic media, such as polystyrene beads, or a filter), and then a solution suspected of containing the binding partner may be applied to the substrate. If a binding partner which can interact with cancer associated antigen polypeptides is present in the solution,

then it will bind to the substrate-bound cancer associated antigen polypeptide. The binding partner then may be isolated.

It will also be recognized that the invention embraces the use of the cancer associated antigen cDNA sequences in expression vectors, as well as to transfect host cells and cell lines, be these prokaryotic (e.g., *E. coli*), or eukaryotic (e.g., dendritic cells, B cells, CHO cells, COS cells, yeast expression systems and recombinant baculovirus expression in insect cells). Especially useful are mammalian cells such as human, mouse, hamster, pig, goat, primate, etc. They may be of a wide variety of tissue types, and include primary cells and cell lines. Specific examples include keratinocytes, peripheral blood leukocytes, bone marrow stem cells and embryonic stem cells. The expression vectors require that the pertinent sequence, i.e., those nucleic acids described *supra*, be operably linked to a promoter.

The invention also contemplates delivery of nucleic acids, polypeptides or peptides for vaccination. Delivery of polypeptides and peptides can be accomplished according to standard vaccination protocols which are well known in the art. In another embodiment, the delivery of nucleic acid is accomplished by *ex vivo* methods, i.e. by removing a cell from a subject, genetically engineering the cell to include a breast cancer associated antigen, and reintroducing the engineered cell into the subject. One example of such a procedure is outlined in U.S. Patent 5,399,346 and in exhibits submitted in the file history of that patent, all of which are publicly available documents. In general, it involves introduction *in vitro* of a functional copy of a gene into a cell(s) of a subject, and returning the genetically engineered cell(s) to the subject. The functional copy of the gene is under operable control of regulatory elements which permit expression of the gene in the genetically engineered cell(s). Numerous transfection and transduction techniques as well as appropriate expression vectors are well known to those of ordinary skill in the art, some of which are described in PCT application WO95/00654. *In vivo* nucleic acid delivery using vectors such as viruses and targeted liposomes also is contemplated according to the invention.

In preferred embodiments, a virus vector for delivering a nucleic acid encoding a cancer associated antigen is selected from the group consisting of adenoviruses, adeno-associated viruses, poxviruses including vaccinia viruses and attenuated poxviruses, Semliki Forest virus, Venezuelan equine encephalitis virus, retroviruses, Sindbis virus, and Ty virus-like particle. Examples of viruses and virus-like particles which have been used to deliver exogenous nucleic acids include:

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replication-defective adenoviruses (e.g., Xiang et al., Virology 219:220-227, 1996; Eloit et al., J. Virol 7:5375-5381, 1997; Chengalvala et al., Vaccine 15:335-339, 1997), a modified retrovirus (Townsend et al., J. Virol. 71:3365-3374, 1997), a nonreplicating retrovirus (Irwin et al., J. Virol. 68:5036-5044, 1994), a replication defective Semliki Forest virus (Zhao et al., Proc. Natl. Acad. Sci. USA 92:3009-3013, 1995), canarypox virus and highly attenuated vaccinia virus derivative (Paoletti, Proc. Natl. Acad. Sci. USA 93:11349-11353, 1996), non-replicative vaccinia virus (Moss, Proc. Natl. Acad. Sci. USA 93:11341-11348, 1996), replicative vaccinia virus (Moss, Dev. Biol. Stand. 82:55-63, 1994), Venzuelan equine encephalitis virus (Davis et al., J. Virol. 70:3781-3787, 1996), Sindbis virus (Pugachev et al., Virology 212:587-594, 1995), and Ty virus-like particle (Allsopp et al., Eur J. Immunol 26:1951-1959, 1996). In preferred embodiments, the virus vector is an adenovirus.

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Another preferred virus for certain applications is the adeno-associated virus, a double-stranded DNA virus. The adeno-associated virus is capable of infecting a wide range of cell types and species and can be engineered to be replication-deficient. It further has advantages, such as heat and lipid solvent stability, high transduction frequencies in cells of diverse lineages, including hematopoietic cells, and lack of superinfection inhibition thus allowing multiple series of transductions. The adeno-associated virus can integrate into human cellular DNA in a site-specific manner, thereby minimizing the possibility of insertional mutagenesis and variability of inserted gene expression. In addition, wild-type adeno-associated virus infections have been followed in tissue culture for greater than 100 passages in the absence of selective pressure, implying that the adeno-associated virus genomic integration is a relatively stable event. The adeno-associated virus can also function in an extrachromosomal fashion.

In general, other preferred viral vectors are based on non-cytopathic eukaryotic viruses in which non-essential genes have been replaced with the gene of interest. Non-cytopathic viruses include retroviruses, the life cycle of which involves reverse transcription of genomic viral RNA into DNA with subsequent proviral integration into host cellular DNA. Adenoviruses and retroviruses have been approved for human gene therapy trials. In general, the retroviruses are replication-deficient (i.e., capable of directing synthesis of the desired proteins, but incapable of manufacturing an infectious particle). Such genetically altered retroviral expression vectors have general utility for the high-efficiency transduction of genes *in vivo*. Standard protocols for

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producing replication-deficient retroviruses (including the steps of incorporation of exogenous genetic material into a plasmid, transfection of a packaging cell lined with plasmid, production of recombinant retroviruses by the packaging cell line, collection of viral particles from tissue culture media, and infection of the target cells with viral particles) are provided in Kriegler, M., "Gene Transfer and Expression, A Laboratory Manual," W.H. Freeman C.O., New York (1990) and Murry, E.J. Ed. "Methods in Molecular Biology," vol. 7, Humana Press, Inc., Cliffton, New Jersey (1991).

Preferably the foregoing nucleic acid delivery vectors: (1) contain exogenous genetic material that can be transcribed and translated in a mammalian cell and that can induce an immune response in a host, and (2) contain on a surface a ligand that selectively binds to a receptor on the surface of a target cell, such as a mammalian cell, and thereby gains entry to the target cell.

Various techniques may be employed for introducing nucleic acids of the invention into cells, depending on whether the nucleic acids are introduced in vitro or in vivo in a host. Such techniques include transfection of nucleic acid-CaPO<sub>4</sub> precipitates, transfection of nucleic acids associated with DEAE, transfection or infection with the foregoing viruses including the nucleic acid of interest, liposome mediated transfection, and the like. For certain uses, it is preferred to target the nucleic acid to particular cells. In such instances, a vehicle used for delivering a nucleic acid of the invention into a cell (e.g., a retrovirus, or other virus; a liposome) can have a targeting molecule attached thereto. For example, a molecule such as an antibody specific for a surface membrane protein on the target cell or a ligand for a receptor on the target cell can be bound to or incorporated within the nucleic acid delivery vehicle. Preferred antibodies include antibodies which selectively bind a cancer associated antigen, alone or as a complex with a MHC molecule. Especially preferred are monoclonal antibodies. Where liposomes are employed to deliver the nucleic acids of the invention, proteins which bind to a surface membrane protein associated with endocytosis may be incorporated into the liposome formulation for targeting and/or to facilitate uptake. Such proteins include capsid proteins or fragments thereof tropic for a particular cell type. antibodies for proteins which undergo internalization in cycling, proteins that target intracellular localization and enhance intracellular half life, and the like. Polymeric delivery systems also have been used successfully to deliver nucleic acids into cells, as is known by those skilled in the art. Such systems even permit oral delivery of nucleic acids.

When administered, the therapeutic compositions of the present invention can be

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administered in pharmaceutically acceptable preparations. Such preparations may routinely contain pharmaceutically acceptable concentrations of salt, buffering agents, preservatives, compatible carriers, supplementary immune potentiating agents such as adjuvants and cytokines and optionally other therapeutic agents.

The therapeutics of the invention can be administered by any conventional route, including injection or by gradual infusion over time. The administration may, for example, be oral, intravenous, intraperitoneal, intramuscular, intracavity, subcutaneous, or transdermal. When antibodies are used therapeutically, a preferred route of administration is by pulmonary aerosol. Techniques for preparing aerosol delivery systems containing antibodies are well known to those of skill in the art. Generally, such systems should utilize components which will not significantly impair the biological properties of the antibodies, such as the paratope binding capacity (see, for example, Sciarra and Cutie, "Aerosols," in Remington's Pharmaceutical Sciences, 18th edition, 1990, pp 1694–1712; incorporated by reference). Those of skill in the art can readily determine the various parameters and conditions for producing antibody aerosols without resort to undue experimentation. When using antisense preparations of the invention, slow intravenous administration is preferred.

The compositions of the invention are administered in effective amounts. An "effective amount" is that amount of a cancer associated antigen composition that alone, or together with further doses, produces the desired response, e.g. increases an immune response to the cancer associated antigen. In the case of treating a particular disease or condition characterized by expression of one or more cancer associated antigens, such as cancer, the desired response is inhibiting the progression of the disease. This may involve only slowing the progression of the disease temporarily, although more preferably, it involves halting the progression of the disease permanently. This can be monitored by routine methods or can be monitored according to diagnostic methods of the invention discussed herein. The desired response to treatment of the disease or condition also can be delaying the onset or even preventing the onset of the disease or condition.

Such amounts will depend, of course, on the particular condition being treated, the severity of the condition, the individual patient parameters including age, physical condition, size and weight, the duration of the treatment, the nature of concurrent therapy (if any), the specific route of

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administration and like factors within the knowledge and expertise of the health practioner. These factors are well known to those of ordinary skill in the art and can be addressed with no more than routine experimentation. It is generally preferred that a maximum dose of the individual components or combinations thereof be used, that is, the highest safe dose according to sound medical judgment. It will be understood by those of ordinary skill in the art, however, that a patient may insist upon a lower dose or tolerable dose for medical reasons, psychological reasons or for virtually any other reasons.

The pharmaceutical compositions used in the foregoing methods preferably are sterile and contain an effective amount of breast cancer associated antigen or nucleic acid encoding cancer associated antigen for producing the desired response in a unit of weight or volume suitable for administration to a patient. The response can, for example, be measured by determining the immune response following administration of the cancer associated antigen composition via a reporter system as described herein, by measuring downstream effects such as gene expression, or by measuring the physiological effects of the breast cancer associated antigen composition, such as regression of a tumor or decrease of disease symptoms. Other assays will be known to one of ordinary skill in the art and can be employed for measuring the level of the response.

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The doses of cancer associated antigen compositions (e.g., polypeptide, peptide, antibody, cell or nucleic acid) administered to a subject can be chosen in accordance with different parameters, in particular in accordance with the mode of administration used and the state of the subject. Other factors include the desired period of treatment. In the event that a response in a subject is insufficient at the initial doses applied, higher doses (or effectively higher doses by a different, more localized delivery route) may be employed to the extent that patient tolerance permits.

In general, for treatments for eliciting or increasing an immune response, doses of cancer associated antigen are formulated and administered in doses between 1 ng and 1 mg, and preferably between 10 ng and 100  $\mu$ g, according to any standard procedure in the art. Where nucleic acids encoding cancer associated antigen of variants thereof are employed, doses of between 1 ng and 0.1 mg generally will be formulated and administered according to standard procedures. Other protocols for the administration of cancer associated antigen compositions will be known to one of ordinary skill in the art, in which the dose amount, schedule of injections, sites of injections, mode of administration (e.g., intra-tumoral) and the like vary from the foregoing. Administration of cancer

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associated antigen compositions to mammals other than humans, e.g. for testing purposes or veterinary therapeutic purposes, is carried out under substantially the same conditions as described above.

As part of the immunization compositions, the peptide antigens are administered with one or more adjuvants to induce an immune response or to increase an immune response. An adjuvant is a substance incorporated into or administered with antigen which potentiates the immune response. Adjuvants may enhance the immunological response by providing a reservoir of antigen (extracellularly or within macrophages), activating macrophages and stimulating specific sets of lymphocytes. Adjuvants of many kinds are well known in the art. Specific examples of adjuvants include monophosphoryl lipid A (MPL, SmithKline Beecham), a congener obtained after purification and acid hydrolysis of Salmonella minnesota Re 595 lipopolysaccharide; saponins including QS21 (SmithKline Beecham), a pure QA-21 saponin purified from Quillja saponaria extract; DQS21, described in PCT application WO96/33739 (SmithKline Beecham); QS-7, QS-17, QS-18, and QS-L1 (So et al., Mol. Cells 7:178-186, 1997); incomplete Freund's adjuvant; complete Freund's adjuvant; montanide; and various water-in-oil emulsions prepared from biodegradable oils such as squalene and/or tocopherol. Other adjuvants are known in the art and can be used in the invention (see, e.g. Goding, Monoclonal Antibodies: Principles and Practice, 2nd Ed., 1986). Methods for the preparation of mixtures or emulsions of peptide and adjuvant are well known to those of skill in the art of vaccination.

Where cancer associated antigen peptides are used for vaccination, modes of administration which effectively deliver the cancer associated antigen and adjuvant, such that an immune response to the antigen is increased, can be used. For administration of a cancer associated antigen peptide in adjuvant, preferred methods include intradermal, intravenous, intramuscular and subcutaneous administration. Although these are preferred embodiments, the invention is not limited by the particular modes of administration disclosed herein. Standard references in the art (e.g., Remington's Pharmaceutical Sciences, 18th edition, 1990) provide modes of administration and formulations for delivery of immunogens with adjuvant or in a non-adjuvant carrier.

When administered, the pharmaceutical preparations of the invention are applied in pharmaceutically-acceptable amounts and in pharmaceutically-acceptable compositions. The term "pharmaceutically acceptable" means a non-toxic material that does not interfere with the

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effectiveness of the biological activity of the active ingredients. Such preparations may routinely contain salts, buffering agents, preservatives, compatible carriers, and optionally other therapeutic agents. When used in medicine, the salts should be pharmaceutically acceptable, but nonpharmaceutically acceptable salts may conveniently be used to prepare pharmaceuticallyacceptable salts thereof and are not excluded from the scope of the invention. Such pharmacologically and pharmaceutically-acceptable salts include, but are not limited to, those prepared from the following acids: hydrochloric, hydrobromic, sulfuric, nitric, phosphoric, maleic, acetic, salicylic, citric, formic, malonic, succinic, and the like. Also, pharmaceutically-

acceptable salts can be prepared as alkaline metal or alkaline earth salts, such as sodium.

potassium or calcium salts.

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A breast cancer associated antigen composition may be combined, if desired, with a pharmaceutically-acceptable carrier. The term "pharmaceutically-acceptable carrier" as used herein means one or more compatible solid or liquid fillers, diluents or encapsulating substances which are suitable for administration into a human. The term "carrier" denotes an organic or 15 inorganic ingredient, natural or synthetic, with which the active ingredient is combined to facilitate the application. The components of the pharmaceutical compositions also are capable of being co-mingled with the molecules of the present invention, and with each other, in a manner such that there is no interaction which would substantially impair the desired pharmaceutical efficacy.

The pharmaceutical compositions may contain suitable buffering agents, including: acetic acid in a salt; citric acid in a salt; boric acid in a salt; and phosphoric acid in a salt.

The pharmaceutical compositions also may contain, optionally, suitable preservatives, such as: benzalkonium chloride; chlorobutanol; parabens and thimerosal.

The pharmaceutical compositions may conveniently be presented in unit dosage form and may be prepared by any of the methods well-known in the art of pharmacy. All methods include the step of bringing the active agent into association with a carrier which constitutes one or more accessory ingredients. In general, the compositions are prepared by uniformly and intimately bringing the active compound into association with a liquid carrier, a finely divided solid carrier, or both, and then, if necessary, shaping the product.

Compositions suitable for oral administration may be presented as discrete units, such as

capsules, tablets, lozenges, each containing a predetermined amount of the active compound. Other compositions include suspensions in aqueous liquids or non-aqueous liquids such as a syrup, elixir or an emulsion.

Compositions suitable for parenteral administration conveniently comprise a sterile aqueous or non-aqueous preparation of breast cancer associated antigen polypeptides or nucleic acids, which is preferably isotonic with the blood of the recipient. This preparation may be formulated according to known methods using suitable dispersing or wetting agents and suspending agents. The sterile injectable preparation also may be a sterile injectable solution or suspension in a non-toxic parenterally-acceptable diluent or solvent, for example, as a solution in 1,3-butane diol. Among the acceptable vehicles and solvents that may be employed are water, Ringer's solution, and isotonic sodium chloride solution. In addition, sterile, fixed oils are conventionally employed as a solvent or suspending medium. For this purpose any bland fixed oil may be employed including synthetic mono-or di-glycerides. In addition, fatty acids such as oleic acid may be used in the preparation of injectables. Carrier formulation suitable for oral, subcutaneous, intravenous, intramuscular, etc. administrations can be found in *Remington's Pharmaceutical Sciences*, Mack Publishing Co., Easton, PA.

#### Examples

## Example 1: Preparation of breast cancer cDNA expression libraries

Step 1: Purification of total RNA from tumors.

Total RNA was isolated from tumor samples using the guanidium thiocyanatephenol-chloroform extraction protocol described by Chomczynski and Sacci (*Anal. Biochem.* 162:156-159, 1987).

Step 2: Purification of mRNA.

A Dynabeads mRNA isolation kit (Dynal, Cat.No. 610.01) was used to isolate mRNA from the pool of total RNA isolated in step 1 above according to the manufacturer's instructions.

Step 3: cDNA synthesis.

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cDNA synthesis was performed using a ZAP-cDNA synthesis Kit (Stratagene, La Jolla CA; Cat. No. 200400) according to the manufacturer's protocol. A specific linker-primer which contains a XbaI cloning site was designed and used in this protocol, to facilitate subcloning into TriplEx

vector. The sequence of the primer was:

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Step 4: Ligation into the TriplEx vector arms.

The cDNAs generated in step 3 above were ligated into TriplEx vector arms (Clontech, Palo Alto, CA; Cat. No. 6162-1); the arms were predigested with EcoR I/Xba I.

Step 5: Packaging into phages with Gigapack III kit.

The ligation mix (TriplEx/cDNA) from step 4 was packed into phages using the Gigapack III Gold Cloning Kit (Stratagene, Cat. N.200450) according to the protocol supplied with the kit.

Step 6: Titering and amplification of generated libraries was performed according to the Stratagene protocols.

The foregoing protocol was used to prepare several libraries from tumor sample of different patients. Some libraries were prepared using the UNI-ZAP XR vector system (Stratagene) according to the manufacturer's protocol, and some using the TriplEx system as described above.

Table 2

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UNI-ZAP Libraries		
Code for tumors	Titer of the library	Histopathological diagnosis
HBR173	1.8 x 10 <sup>6</sup> pfu	Ductal Carcinoma, Grade III
HBR184	3.5 x 10 <sup>6</sup> pfu	Invasive Ductal Carcinoma, Grade II
TriplEx libraries		
Code for tumors	Titer of the library	Histopoathological diagnosis
HBR173	2.3 x 10 <sup>6</sup> pfu	Ductal Carcinoma, Grade III
HBR184	1.1 x 10 <sup>6</sup> pfu	Ivasive Ductal Carcinoma, Grade II
HBR257	2.5 x 10 <sup>6</sup> pfu	Invasive Ductal Carcinoma, Grade II
HBR297	4.0 x 10 <sup>6</sup> pfu	Ductal Carcinoma, Grade II
HBR248	1.0 x 10 <sup>6</sup> pfu	Invasive Ductal Carcinoma with
		Vascular Permeation, Grade III

HBR271	2.5 x 10 <sup>6</sup> pfu	Medullary Carcimoma
HBR263	10.0 x 10 <sup>6</sup> pfu	Inv. Pleiomorphic Lobular Carcinoma,
		Grade II

All libraries were screened with the exception of HBR173 (no autologous serum). No serum-positive clones were found by screening HBR271 library.

#### **Example 2: Immunoscreening**

Sera was obtained from donors undergoing routine diagnostic and therapeutic procedures. It was stored at - 70°C prior to absorption. Sera, at a dilution of 1:10 in Tris buffered saline (TBS, pH 7.5), was sequentially passed through Sepharose 4B columns which had been coupled to lysates from E. coli Y1090 and bacteriophage infected E. coli BNN97 (5 Prime 3 Prime, Inc. Boulder, Co.). Final serum dilutions were prepared in 0.2% non-fat dried milk/TBS (NFDM) and stored at 4°C. Library screening was performed as described by Sahin et al. (Proc. Natl. Acad. Sci. USA 92:11810-11813, 1995) with following modifications. Recombinant phage at a concentration of 4 x 10<sup>3</sup> per 15 cm plate were amplified for 6 hours and transferred to nitrocellulose membranes for an additional 15 hours at 37°C. Membranes were then blocked with 5% NFDM. As an alternative to generation of IgG subtracted libraries, membranes were pre-screened in a 1:2000 dilution of peroxidase conjugated, Fc fragment specific, goat anti-human IgG (Jackson Immunoresearch Laboratories Inc., West Grove, PA) for 1 hour at room temperature. Color was developed with 3,3' diaminobenzidine tetrahydrochloride and IgG encoding clones were scored. Membranes were then incubated in a 1:100 dilution of absorbed autologous sera for 15 hours at room temperature. Following serum exposure, filters were incubated in a 1:3000 dilution of alkaline phosphatase conjugated, Fc fragment specific, goat anti-human IgG (Jackson Immunoresearch Laboratories Inc.) for 1 hour at room temperature and processed for 4-nitro blue tetrazolium chloride/5-bromo-4-chloro- 3-indolyl-phosphate color development. Serum positive clones were subcloned and retested for serum reactivity as above except nitrocellulose transfer was decreased to 3 hours. For the determination of allogeneic serum reactivity, plates containing an equal number of serum positive clones and negative control plaques were similarly processed less the IgG prescreening steps. A minimum of 5 x 10<sup>5</sup> recombinants were screened per cDNA library, a number

which approximates a point at which the likelihood of repeat isolations of previously identified clones outweigh the prospect of identifying new clones.

## **Example 3: DNA Sequencing**

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Phage cDNA clones were converted to pBKCMV phagemid forms by in vivo excision. Plasmid DNA was purified on Qiaprep spin columns (Qiagen Inc. Chatsworth, CA) and subjected to EcoRI/XbaI restriction enzyme digestion. Clones representing different cDNA inserts were sequenced at Cornell University DNA services (Ithaca, NY) using an ABI Prism (Perkin Elmer) automated DNA sequencer. The sequences of the clones were compared with sequences in 10 GenBank and HGI databases to detect homologous nucleic acid and/or protein sequences. The following table lists exemplary related sequences.

Table 3: Sequences Related to Breast Cancer Associated Antigen Clones

	Clone	Nucleotide Homology	Clone	Nucleotide Homology	Clone	Nucleotide Homology
15	LONY-Br-1	L34543	LONY-Br-23	AA262134, U74628	LONY-Br-44	D15057
	LONY-Br-2	S75417	LONY-Br-24	AA282633	LONY-Br-45	AB000815
	LONY-Br-3	J05211	LONY-Br-25	M62324	LONY-Br-46	L04733
	LONY-Br-4	X15187	LONY-Br-26	M99389	LONY-Br-47	X88791
	LONY-Br-5	X62083	LONY-Br-27	X79389	LONY-Br-48	AF000430
20	LONY-Br-6	J04965	LONY-Br-28	D44466	LONY-Br-49	none
	LONY-Br-7	D63784	LONY-Br-29	M33197	LONY-Br-50	AA226732
	LONY-Br-8	U11292	LONY-Br-30	M17886	LONY-Br-51	AA046574
	LONY-Br-9	HSB06D102	LONY-Br-31	L38941	LONY-Br-52	none
	LONY-Br-10	none	LONY-Br-32	X17644	LONY-Br-53	AB002307
25	LONY-Br-11	none	LONY-Br-33	X75342	92	AA127328
	LONY-Br-12	AA430998	LONY-Br-33	X75342	101	AA167314
	LONY-Br-13	D83032	LONY-Br-34	U43368	102	AA508139
	LONY-Br-14	AA034417	LONY-Br-35	X15882	107	none
	LONY-Br-15	AA167070	LONY-Br-37	AA121558	109	AA220229

LONY-Br-16	none	LONY-Br-38	AA211771	110	W67775
LONY-Br-17	AA161103	LONY-Br-39	AA367417	111 .	AA280070
LONY-Br-19	R13835	LONY-Br-40	AA188052	112	AF004292
LONY-Br-20	HUMORF003	LONY-Br-41	THC83518	131	none
LONY-Br-21	S74572	LONY-Br-42	none	143	AA481578
LONY-Br-22	AA070233	LONY-Br-43	HU35246	162	AA481578

## Example 4: Reverse transcriptase (RT) PCR and Rapid Amplification of cDNA Ends (RACE)

The mRNA expression pattern of selected cDNA clones was determined by RT- PCR using a panel of normal tissue RNA. This test panel consisted of lung, testis, small intestine, colon, breast, liver, and placenta, and was purchased from Clontech Laboratories Inc. (Palo Alto, CA). Colon tumor RNA was also included in this panel and was prepared as described above. As a control for genomic DNA contamination, all cDNA synthesis reactions were set up in duplicate with the additional sample lacking reverse transcriptase. Gene specific PCR primers were designed to amplify 5' fragments of 300-400 bp and were purchased commercially (Gibco BRL, Grand Island, NY). PCR reactions were undertaken at an annealing temperature of 68°C using a Perkin Elmer thermal cycler. In certain cases, RT-PCR products were subcloned into the pCR2.1 plasmid vector (Invitrogen) and multiple clones were subjected to DNA sequencing as described. 5' and 3' RACE reactions were undertaken using gene specific and adapter primers in conjunction with Marathon Ready normal colon cDNA and KlenTaq polymerase (Clontech) as per manufacturers protocol. Products were then subcloned into the pCR2.1 plasmid vector (Invitrogen) and screened by PCR with internal primers for presence of the desired insert. Multiple RACE clones were subjected to DNA sequencing as described.

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## Example 5: Northern blot analysis

Northern blots containing the transfer yields of 2  $\mu$ g poly A<sup>+</sup> RNA from a panel of normal tissues were obtained commercially (Clontech). Random primed <sup>32</sup>P labeled probes consisting of 300-600 bp PCR products from 5 prime coding sequences of serum positive cDNA clones were hybridized for 1.5 hours in Expresshyb (Clontech) at 68 °C and washed at high stringency (2 times,

30 min. each, 0.1X SSC/0.1% SDS at 68°C). Resultant blots were used to expose Biomax MS autoradiography film (Eastman Kodak Co., Rochester, NY).

Table 4: Breast Cancer Associated Antigen Clone mRNA sizes

5	Clone	Size (kb)	Clone	Size (kb)	Clone	Size (kb)
	LONY-Br-1	1.8	LONY-Br-17	1.0	LONY-Br-33	2.6
	LONY-Br-2	2.9	LONY-Br-19	1.5	LONY-Br-34	2.1
	LONY-Br-3	4.8	LONY-Br-20	2.4	LONY-Br-35	1.9
	LONY-Br-4	1.2	LONY-Br-21	2.4	LONY-Br-36	0.8
10	LONY-Br-5	0.9	LONY-Br-22	1.6	LONY-Br-37	1.0
	LONY-Br-6	1.4	LONY-Br-23	1.3	LONY-Br-38	2.2
	LONY-Br-7	1.3	LONY-Br-24	3.9	LONY-Br-39	1.9
	LONY-Br-8	0.9	LONY-Br-25	1.9	LONY-Br-40	3.4
	LONY-Br-9	6.0	LONY-Br-26	1.5	LONY-Br-41	3.9
15	LONY-Br-10	3.6	LONY-Br-27	1.2	LONY-Br-42	0.6
	LONY-Br-11	4.6	LONY-Br-28	0.5	LONY-Br-43	1.4
	LONY-Br-12	2.2	LONY-Br-29	0.6	LONY-Br-44	0.7
	LONY-Br-13	1.2	LONY-Br-30	0.8	LONY-Br-45	3.0
	LONY-Br-14	0.8	LONY-Br-31	0.4	LONY-Br-46	3.7
20	LONY-Br-15	0.9	LONY-Br-32	2.2	LONY-Br-47	0.5
	LONY-Br-16	2.5	LONY-Br-33	2.6	LONY-Br-48	1.6

## Example 6: Isolation of gastric and prostate clones

A stomach cancer cDNA library was established, using standard techniques, then the library was screened, using the SEREX methodology described supra, and set forth by Sahin et al., *Proc. Natl. Acad. Sci. USA* 92: 11810 (1995), and by Chen et al., *Proc. Natl. Acad. Sci. USA* 94: 1914 (1997), incorporated by reference in their entirety.

To be specific, total RNA was isolated by homogenizing tumor samples in 4M guanidium thiocyanate/0.5% sodium N-lauryl sarcosine/ and 25 mM EDTA followed by centrifugation in 5.7 M CsCl/25 mM sodium acetate/10 uM EDTA at 320,000 rpm. Total mRNA was removed by passing the sample over an oligo-dT cellulose column. The cDNA libraries were then constructed

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by taking 5 ug of mRNA, using standard methodologies to reverse transcribe the material.

Libraries were prepared from four different stomach cancer patients, referred to as "SM", "CK" and "SS" and "KM" respectively. A total of 2.5x10<sup>6</sup>, 1.1x10<sup>6</sup>, and 1.7x10<sup>6</sup> cDNA clones were obtained from the "SM", "CK" and "SS" individuals. Additional libraries were prepared from prostate cancer patient "OT".

The cDNA was used to construct a lambda phage library, and 500 phages were plated onto XL1-Blue MRF E. coli, and incubated for eight hours at 37°C. A nitrocellulose membrane was then placed on the plate, followed by overnight incubation. The membrane was then washed, four times, without TBS which contained 0.05% Tween, and was then immersed in TBS containing 5% non-fat dried milk. After one hour, the membrane was incubated with conjugates of peroxidase-goat anti human IgG specific for Fc portions of huma antibody (1:2000, diluted in TBS with 1% BSA. The incubation was carried out for one hour, at room temperature, and the membrane was then washed three times with TBS. Those clones which produced antibodies were visualized with 0.06%, 3,3'diamino benzidine tetrachloride, and 0.015% H<sub>2</sub>O<sub>2</sub>, in 50 mM Tris (pH 7.5). Any clones which produced immunoglobulin were marked, and then the membrane was washed, two further times, with TBS that contained 0.05% Tween, and then twice with "neat" TBS.

The membranes were then incubated in 1:100 diluted patient serum, overnight, at 4°C. The patient serum had been pretreated. Specifically, 5 ml samples were diluted to 10 ml with TBS containing 1% bovine serum albumin, and 0.02% Na<sub>3</sub>N. The serum had been treated to remove antibodies to bacteriophage, by passing it through a 5 ml Sepharose column, to which a lysate of E. coli Y1090 had been attached, followed by passage over a second column which had E. coli lysate and lysate of E. coli infected with lambda bacteriophage. The screening was carried out five time. The samples were then diluted to 50 ml, and kept at -80°C, until used as described herein.

Following the overnight incubation with the membrane, the membrane was washed twice with TBS/0.05% Tween 20, and then once with TBS. A further incubation was carried out, using the protocols discussed supra, for the POD labelled antibodies.

The positive clones were then sequenced, using standard techniques. Following comparison of the sequences to information available in data banks, a total of 36 clones were resolved into known and unknown genes. In the table that follows, the "+" and "-" signs are essentially used to compare signals to each other. All were positive. Table 5, which follows, summarizes some of this

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work isolation and sequencing of "SM" clones. Specifically, with reference to the first page of the table, previously identified human proteins and the nucleotide sequences, set forth in SEQ ID NOS:588-626 are known. The four molecules which follow in SEQ ID NOS:627-634 (gelsolin, zinc finger protein family, variant zinc finger motif protein goliath and homeodomain proteins), have not been identified in humans previously, although there are related molecules found in other species. Finally, with reference to Table 5, the last four moieties, i.e., prepro-α collagen, heterogeneous ribonucleoprotein D, nucleosome assembly protein 2, and NY-ESO-2/Ulsn NRP/V1 small nuclear ribonucleoprotein, are also known. Nucleotide sequences are set forth at SEQ ID NOS:635-642. The nucleic acid molecules having the nucleotide sequences set forth at SEQ ID NOS:643-670 represent molecules for which no related sequences were found. SEQ ID NO:671 combines the sequences of SEQ ID NOS:627-630, inclusive. SEQ ID NO:672 combines SEQ ID NOS:643-656, SEQ ID NO:673 combines SEQ ID NOS:657, 659 and 662, while SEQ ID NO:674 combines SEQ ID NOS:658, 660, 661 and 663.

SEREX analysis of clones from libraries derived from patients "CK", "SS", "KM" (all gastric cancer) and patient "OT" (prostate cancer) was carried out as described above. The nucleotide sequences of clones derived from gastric cancer patients are presented as SEQ ID Nos:176-436. The nucleotide sequences of clones derived from prostate cancer patient "OT" are presented as SEQ ID Nos:437-543.

#### 20 Example 7: Isolation and analysis of colon clones

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Colon tumor samples were obtained as surgical samples, and were frozen at -80°C until ready for use.

Total RNA was then isolated from the samples, using the guanidium thiocyanate method of Chirgwin, et al., *Biochemistry* 18: 5294-5299 (1979), incorporated by reference. The total RNA thus obtained was then purified to isolate all poly A<sup>+</sup> RNA, using commercially available products designed for this purpose.

The poly A<sup>+</sup> RNA was then converted into cDNA, and ligated into  $\lambda$ ZAP, a commercially available expression vector, according to the manufacturer's suggested protocol.

Three cDNA libraries were constructed in this way, using colorectal carcinoma samples.

A fourth library, also from colorectal carcinoma, was prepared, albeit in a different way. The

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FOR amplification of a cDNA clone which encoded an IgG molecule. See, e.g., Ace et al, Endocrinology 134: 1305-1309 (1994), and incorporated by reference in its entirety. IgG subtraction is done to eliminate any false, positive signals resulting from interaction of cDNA clones which encode IgG, with the IgG then interacting with the anti-human IgG used in the SEREX assay, as described herein. PCR products were biotinylated, and hybridized with denatured second strand cDNA, at 68°C for 18 hours. Biotinylated hybrid molecules were coupled to streptavidin, and then removed by phenol chloroform extraction. Any remaining cDNA was also ligated into λZAP. All libraries were amplified, prior to immunoscreening.

Immunoscreening was carried out using sera obtained from patients undergoing routine diagnostic and therapeutic procedures. The sera were stored at -70°C prior to use. Upon thawing, the sera were diluted at 1:10 in Tris buffered saline (pH 7.5), and were then passed through Sepharose 4B columns. First, the sera were passed through columns which had <u>E. coli</u> Y1090 lysates coupled thereto, and then lysates from bacteriophage infected <u>E. coli</u> BNN97 lysates. Final serum dilutions were then prepared in 0.2% non-fat dried milk/Tris buffered saline.

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The method of Sahin et al., *Proc. Natl. Acad. Sci. USA* 92:11810-11813 (1995), and U.S. Patent No. 5,698,396, both of which are incorporated by reference, was used, with some modifications. Specifically, recombinant phages at a concentration of 4x10<sup>3</sup> phages per 15 cm plate (pfus), were amplified for six hours, after which they were transferred to nitrocellulose membranes for 15 hours. The membranes then were blocked with 5% nonfat dried milk.

As an alternative to the IgG subtraction procedure discussed above, membranes were prescreened in a 1:2000 dilution of peroxidase conjugated, Fc fragment specific goat anti-human IgG, for one hour, at room temperature. Color was developed using 3,3'-diaminobenzidine tetrahydrochloride, which permitted scoring of IgG encoding clones.

Membranes were then incubated in 1:100 dilutions of autologous sera, which had been pretreated with the Sepharose 4B columns, as described <u>supra</u>. The filters were then incubated, in a 1:3000 dilution of alkaline phosphatase conjugated Fc fragment specific, goat anti-human IgG, for one hour, at room temperature. The indicator system 4-nitroblue tetrazolium chloride/5-bromo-4-chloro-3-indolyl-phosphate was then added, and color development assessed. Any positive clones were subcloned, and retested, except the time on the nitrocellulose membrane was reduced to three

hours.

Positive clones were isolated and sequenced according to standard procedures. The nucleotide sequences of the clones are set forth in the even numbered sequences from SEQ ID Nos:544-586. The odd numbered sequences from SEQ ID Nos:545-587 represent the translated amino acid sequences of the colon nucleic acid clones. Analysis of probes for SEQ ID NOS:544 and 546 confirmed their universal expression.

The foregoing results reflect SEREX isolation of colon cancer clones using autologous serum. The positive clones were then rescreened, using allogeneic serum, following the same method discussed supra, in example 2, except IgG prescreening was omitted. The allogeneic sera was obtained from sixteen normal blood donors, and twenty nine patients who had been diagnosed with colorectal cancer.

The analysis with the two types of serum revealed that fourteen reacted with a subset of sera from normal and cancer patients, twenty-eight only with autologous sera, and six with both allogeneic and autologous sera. Over 60% of the allogeneic serum samples tested reacted with at least one of these positive clones. About 20% reacted with two or more.

In view of the results described above, further experiments were carried out using serum samples from patients with other forms of cancer, i.e., renal cancer (13 samples), lung cancer (23 samples), and breast cancer (10 samples). The results are set forth in Table 6 which follows:

20 Table 6: Allogeneic serotyping using colon cancer clones

Clone Number	Normal Sera	Colon Cancer	Renal Cancer	Lung Cancer	Breast Cancer
NY-Co-8	0/16	8/29	1/13	0/23	0/10
NY-Co-9	0/16	5/29	1/13	1/23	0/10
NY-Co-13	0/16	5/29	0/13	0/23	0/10
NY-Co-16	0/16	3/29	0/13	0/23	0/10
NY-Co-20	0/16	4/29	0/13	0/23	0/10
NY-Co-38	0/16	4/29	3/13	0/23	1/10

Of the six clones which were identified as being reactive with autologous and allogeneic

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cancer serum, and not with normal serum, two were found to be identical to previously identified molecules (NY-Co-. Four others were found to have little or no homology to known sequences and thus are preferred allogeneic-reactive colon cancer clones. These nucleic acids and their polypeptide translations are presented as SEQ ID NOS: 544-551: SEQ ID NO: 544/545 (NY-CO-8), SEQ ID NO: 546/547 (NY-CO-9), SEQ ID NO: 548/549 (NY-CO-16) and SEQ ID NO: 550/551 (NY-CO-38). Of twenty seven allogeneic colon cancer serum samples tested, 67% reacted with at least one of these antigens.

The expression pattern of mRNA corresponding to SEQ ID NOS:544, 546 and 550, as well as other sequences identified via the preceding examples was determined. To do this, RT-PCR was carried out on a panel of RNA samples, taken from normal tissue. The panel contained RNA of lung, testis, small intestine, colon, breast, liver and placenta tissues. The RNA was purchased from a commercial source. RNA from a colon tumor sample was also included. All samples were set up for duplicate runs, so that genomic DNA contamination could be accounted for. In the controls, no reverse transcriptase was used.

Primers were designed which were specific for the cDNA, which would amplify 5'-fragments, from 300-400 base pairs in length. The PCR reactions were undertaken at an annealing temperature of 68°C. Where appropriate, 5' and 3'-RACE reactions were undertaken, using gene specific primers, and adapter primers, together with commercially available reagents. Specifically, SEQ ID NOS: 546 and 550 were tested using RACE. The resulting products were subcloned into vector pCR 2.1, screened via PCR using internal primers, and then sequenced.

SEQ ID NOS:544 and 546 were found to be amplified in all tissues tested. SEQ ID NO:550 was found in colon tumor, colon metastasis, gastric cancer, renal cancer and colon cancer cell lines Colo 204 and HT29, as well as in normal colon, small intestine, brain, stomach, testis, pancreas, liver, lung, heart, fetal brain, mammary gland, bladder, adrenal gland tissues. It is was not found in normal uterine, skeletal muscle, peripheral blood lymphocytes, placental, spleen thymus, or esophagus tissue, nor in lung cancer.

The analysis also identified differential expression of a splice variant of SEQ ID NO:550, i.e., SEQ ID NO:552. When the two sequences were compared, it was found that SEQ ID NO:550 encodes a putative protein of 652 amino acids (SEQ ID NO:551), and molecular weight of 73,337 daltons. SEQ ID NO:552, in contrast, lacks an internal 74 base pairs, corresponding to

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nucleotides 1307-1380 of SEQ ID NO:550. The deletion results in formation of a stop codon at the splice function, and a putative protein of 403 amino acids (SEQ ID NO:553), and molecular weight 45,839. The missing segment results in the putative protein lacking a PEST protein degradation sequence, thereby suggesting a longer half life for this protein.

In additional experiments, primers designed not to differentiate between SEQ ID NOS: 550 and 552 resulted in almost universal amplification (placenta being the only exception). In contrast, when primers specific for SEQ ID NO:552 were used differences were seen in normal pancreatic, liver, lung, heart, fetal brain, mammary gland, bladder, and adrenal gland tissue, where there was no expression of SEQ ID NO:552 found.

Northern blotting was also carried out for SEQ ID NOS: 544, 546, 550 and 552. These experiments employed the same commercially available RNA libraries discussed above were used.

Samples (2 ug) of polyA<sup>+</sup> RNA were analyzed from these samples, using random, <sup>32</sup>P labelled probes 300-360 nucleotides in length, obtained from PCR products. These probes were hybridized to the RNA, for 1.5 hours, at 68°C, followed by two washes at 0.1xSSC, 0.1% SDS, 68°C, for 30 minutes each time.

SEQ ID NOs:544 and 546 were again found to be universally expressed.

Further screening identified additional isoforms of SEQ ID NOS:544 and 550. These are set forth as SEQ ID NOS: 554, 556, 558 and 560. The isoform represented by SEQ ID NO:554 (translated as SEQ ID NO:555) is a naturally occurring splice variant of SEQ ID NO:544, found in normal colon. SEQ ID NO:556 (translated as SEQ ID NO:557), which is an isoform of SEQ ID NO:550 (translated as SEQ ID NO:551), was found in brain tissue, primarily spinal chord and medulla. SEQ ID NO:558 (translated as SEQ ID NO:559), was found in normal kidney and in colon tumors, metastasized colon cancer, renal cancer, gastric cancer, and in colon cancer cell line Colo 205. It was not found in any normal tissue other than kidney.

The nucleic acid molecule whose nucleotide sequence set forth as SEQ ID NO:560 (translated as SEQ ID NO:561), is a further isoform of SEQ ID NO:552. It is similar to SEQ ID NO:558, except it contains a long nucleotide insert encoding a longer COOH terminus. It was expressed in normal bladder and kidney cells, and renal cancer cells. It was not expressed in colon cancer cells.

It is reported above that fourteen clones reacted with subsets of serum from both normal

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and cancer patients, while twenty eight reacted with autologous sera only. These clones were sequenced, in accordance with standard, art recognized methods. Of the clones which reacted only with autologous sera, nine appear to be previously unidentified sequences. These are set forth as SEQ ID NOS: 562, 564, 566, 568, 570, 572, 574, 576 and 578. SEQ ID NO:562 (translated as SEQ ID NO:563) is 1445 nucleotides long, and shows some similarity to known sequences for myosin and tropomyosin. SEQ ID NO:564 (translated as SEQ ID NO:565), which is 1226 nucleotides long, contains a TPR motif. The sequence set forth in SEQ ID NO:566 (translated as SEQ ID NO:567) is 1857 nucleotides long, and shows similarity to cyclophillins. The nucleotide sequence set forth in SEQ ID NO:568 (translated as SEO ID NO:569) is 1537 nucleotides long, and shows similarity to murine gene 22A3, which has unknown function, but resembles an unconventional form of myosin, as well as an EST for heat shock inducible mRNA. As for the molecule set forth in SEQ ID NO:570 (translated as SEQ ID NO:571), it appears to resemble a nucleic targeting signal protein. SEQ ID NO: 572 (translated as SEQ ID NO:573) is 604 nucleotides long, and may encode a lysosymal protein. The molecule set forth in SEO ID NO:574 (translated as SEQ ID NO:575) is 742 nucleotides long, and encodes a protein with an SH3 domain and which shows some similarity to GRB2 and human neutrophil oxidase factor. The molecule set forth in SEQ ID NO:576 (translated as SEQ ID NO:577) is 1087 nucleotides long, and encodes a protein which contains coiled core domains. The molecule set forth in SEO ID NO:578 (translated as SEQ ID NO:579) is 2569 nucleotides long, shows some similarity with Drosophila homeotic material tudor protein, and has a DY(F)GN repeat.

Additional sequences were identified which were expressed in both normal sera and cancer cells. The sequence set forth in SEQ ID NO:580 (translated as SEQ ID NO:581), e.g., is 2077 nucleotides long, and was expressed by both colorectal cancer and normal cells. Analysis of the sequence showed that it possesses a nuclear targeting sequence. The molecule set forth in SEQ ID NO:582 (translated as SEQ ID NO:583) is 3309 nucleotides long, was expressed by colorectal cancer and normal cells, and is similar to heat shock protein 110 family members. The molecule presented in SEQ ID NO:584 (translated as SEQ ID NO:585) was expressed in a colon to lung metastasis, as well as by normal tissue. It is 2918 nucleotides in length. Analysis shows that it contains 2 zinc finger domains. The nucleotide sequence of SEQ ID NO:586 (translated as SEQ ID NO:587) was also expressed in a colon to lung metastasis, is 1898 nucleotides long, and is

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also expressed by normal tissue. Specifically, the reactivity of the molecules was as follows:

Table 7

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5	SEQ ID NO:	Normal Sera Reactivity	Tumor Sera Reactivity
	580	2/16	2/16
	582	2/16	3/16
10	584	2/16	2/16
	586	2/8	1/16

A more extensive set of RT-PCR experiments were carried out to study the expression pattern of SEQ ID NOS: 550, 552, 558 and 560. The results follow.

Table 8: RT-PCR analysis of colon SEREX clones

		SEQ ID	SEQ ID	SEQ ID	SEQ ID
	normal tissue	NO.:550	NO.:552	NO.:558	NO.:560
20	kidney	+	Negative	Negative	Negative
	colon	+	Negative	Negative	Negative
	small		Negative	Negative	Negative
	intest.	+	Negative	Negative	Negative
	brain	+	Negative	Negative	Negative
25	stomach	+	Negative	Negative	Negative
	testis	+	Negative	Negative	Negative
	pancreas	+	Negative	Negative	Negative
	lung	+	Negative	Negative	Negative
	liver	+	Negative	Negative	Negative
30	heart	+	Negative	Negative	Negative
	fetal		Negative	Negative	Negative
	brain	+	Negative	Negative	Negative
	mammary		Negative	Negative	Negative
	gland	+	Negative	Negative	Negative
35	bladder	+	Negative	Negative	Negative
	adrenal		Negative	Negative	Negative
	gland	+	Negative	Negative	Negative
	uterus	Negative	Negative	Negative	Negative
	skeletal		Negative	Negative	Negative
40	muscle	Negative	Negative	Negative	Negative
	PBL	Negative	Negative	Negative	Negative
	placenta	Negative	Negative	Negative	Negative
		=			-

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	spleen thymus esophagus	Negative Negative Negative	Negative Negative Negative	Negative Negative Negative	Negative Negative Negative
	Tumor Tissue				
5	renal cancer (4) colon primary	+ (2/4)	+ (2/4)	+ (2/4)	+ (2/4)
	tumors (10)	+ (10/10)	+ (10/10)	+(10/10)	Negative
10	colon mets (4) breast	+ (4/4)	+ (4/4)	+ (4/4)	Negative
	cancer (6)	+ (3/6)	Negative	Negative	Negative
15	lung cancer (6)	+ (6/6)	Negative	Negative	Negative
	gastric cancer (1)	+	+	+	Not tested
	colon cancer cell lines				
20	colo 205 HT29 HCT15	+ + Negative	+ + Negative	+ Negative Negative	Negative Negative Negative

## Example 8: Isolation and analysis of additional clones

For the establishment of a cDNA library from human tissue total RNA was obtained from
0.5 g of a renal clear cell carcinoma and established according to the method of Chomzynski as
described above The mRNA was extracted from total RNA with oligo-dT-cellulose. The synthesis
of the first strand cDNA was accomplished by the method described by Gubler and Hoffmann, *Gene*25: 263 (1983) using RNase H and DNA polymerase I. For adaptation of the cDNA Klenow
enzyme, adaptors with EcoRI restriction enzyme sites were ligated to the cDNA ends using T4 DNA
ligase (Ferretti L and Sgamerella V, *Nucl. Acids Res.* 9: 3695 (1981)). Following restriction
enzymatic digestion with the enzyme Xhol, cDNA molecules of different length were separated
using Sephacryl 400 and transfected into λZAPII phage vectors (Short JM et al., *Nucleic Acids Res.*16: 7583 (1988)). The recombinant phage DNA was packaged into phages after ligation with
packaging extracts and used for the transfection of *E. coli* bacteria. The titration of the library
resulted in 1.8 x 10<sup>6</sup> recombinant primary clones. The total cDNA library was transfected in *E. coli* and amplified. The titer of the cDNA library after amplification was 10<sup>11</sup> plaque forming units per
ml (pfu/ml). These transfected cells were used in experiments which follow.

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In accordance with the invention as described above, identification of immunogenic material was achieved by using human sera which has been completely depleted of antibodies directed against antigens derived from native and lytic  $\lambda$  phage-transfected  $E.\ coli$  bacteria. To this end, the serum was absorbed, as follows.

 $E.\ coli$  bacteria of the strain XL1-blue were cultured in 50 ml LB medium overnight. After achieving an optical density of  $OD_{600} = 1.0$ , the bacteria were pelleted by centrifugation, resuspended in 5 ml phosphate buffered saline (PBS), and lysed by sonication. The bacterial lysate was bound onto a matrix of activated Sepharose, which was then put into a column and used for the absorption of the human serum. The serum was run over this column 10 times.

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A culture of *E. coli* XL1 blue bacteria in the exponential growth phase was pelleted by centrifugation, transfected in 0.01 M magnesium sulfate with  $10^6 \lambda$ ZAPII phages without a recombinant insert and incubated in 5 ml LB medium for four hours. The lysate of the transfected bacteria was used in the same manner as the untransfected bacteria, with the human serum described supra being passed through the column an addition ten times.

To complete the depletion of the serum, interfering antibodies from lytically transfected *E. coli* bacteria were cultured on agar plates and their proteins were blotted onto nitrocellulose membranes after 10 hours of culture at 37°C. Following this, the serum which had been preabsorbed according to the above steps was transferred to the blotted nitrocellulose membrane, and the absorption procedure was repeated five times. The serum, which was processed in accordance with the invention, was totally depleted of antibodies directed against antigens derived from *E. coli* and phages.

In this, a renal cancer-specific antigen was identified via the following steps. Bacteria of the strain XL1 blue were transfected with recombinant phages derived from the described cDNA library and plated at a density of 4-5x10<sup>3</sup> plaque forming units (pfu) per plate in LB-medium with isopropylthiogalactopyranoside ("IPTG"). After 12 hours of incubation at 37°C, nitrocellulose membranes were put on top of the cultures and culture plates were incubated for another four hours. This was followed by incubation of the nitrocellulose membrane for one hour in Tris-buffered saline (PBS) with 5% milk powder. After washing the nitrocellulose membranes three times in TBS, the stripped human serum secured following Example 2 was diluted 1:1000 in TBS/0.5% (w/v) milk power and incubated overnight with gentle shaking. After the incubation with the nitrocellulose

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membrane the serum was removed and kept for additional testing. Following incubation with serum, the nitrocellulose membranes were washed three times in TBS, and incubated with a polyclonal alkaline phosphatase-conjugated goat anti-human IgG serum for one hour. Following this, the nitrocellulose membranes were washed repeatedly with TBS/0.01% (v/v Tween 20). The reaction was developed using nitroblue tetrazolium chloride and bromochloro-indoyl-phosphate in TBS. The binding of human antibodies to the expressed protein became visible by a blue ringformed color deposit on the nitro-cellulose membrane. The efficient preabsorption of the serum made in possible to develop the membrane at 37°C over several hours without compromising the quality of the test because of background reactivity caused by antibodies against *E. coli* and phage antigens.

Positive clones were localized on the agar plates, transferred into transfection buffer, and used for a second round of transfection and subcloning. A total of 1.8x10<sup>6</sup> recombinant clones were subjected to screening and five different positive-reacting clones were identified.

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Positive clones, i.e., those which had bound antibodies derived from the processed human

serum, were subcloned to monoclonality by repeated rounds of transfection and testing of reactivity
with the processed human serum. P-bluescript phagemids with the respective cDNA inserts were
cloned by in vivo excision (Hay B and Short JM, Strategies 5: 16-19, 1992) from the λZAPII phage
vectors and used for the transfection of E. coli SOLR bacteria. Plasmids were isolated from the
bacteria after alkaline lysis with NaOH in a modification of the method of Birnboim HC and Doly J.

J. Nucl. Acids Res. 7: 1513 (1979). The recombinant plasmid DNA was sequenced according to
standard methods using M13-forward and M13-reverse oligonucleotides. The DNA sequence
obtained and the resulting amino acid sequence were compared with nucleic acid and protein data
banks (Gene Bank, EMBL, Swiss Prot). The sequencing of the cDNA inserts was continued using
internal oligonucleotides. Analysis showed no homology with any sequences deposited in the data
banks. The full length cDNA clone, referred to as SK313, was cloned with the RACE method
(Frohman MA, Dush MK, Martin GR, Proc. Natl. Acad Sci. USA 85: 8998 (1988)), and had a
carbonic anhydrase domain at the 5' end.

As a continuation of these experiments, RNA was isolated from a spectrum of malignant and normal human tissues and Northern blots were performed with labeled SK313 (also referred to as clone HOM-RCC-313). The Norther blot analysis demonstrated that the mRNA of clone HOM-

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RCC-313 was overexpressed in 4 out of 19 renal cell carcinomas compared to normal kidneys. Very weak expression was found only in colonic mucosal tissue and in normal kidney. Expression in other tissues was not observed.

To determine the incidence of antibodies against antigens which are identified above, allogeneic sera from healthy individuals and tumor patients were analyzed. To this end, the sera were processed as described above and depleted from antibodies against antigens derived from *E. coli* and phages. For the detection of antigen-specific antibodies, phages derived from reactive clones were mixed with non-reactive phages derived from the same cDNA library at a ratio of 1:10 and tested as described above for reactivity with antibodies in the human test serum. The serum which had been used for the identification of the antigen was used as a positive control. The non-reactive phages served as a negative control. A serum sample was positive for antigen reactive antibodies, if the expected percentage of the phage plaques showed a positive reaction. In the case of the renal cell carcinoma antigen represented by clone HOM-RCC-313, the analysis of a spectrum of human sera showed that only sera from renal cell carcinoma patients contained reactive antibodies. Sera from healthy controls and patients with other tumors did not contain such antibodies.

The cDNA for clone HOM-RCC-313 was excised from the plasmid DNA by digestion with the restriction enzyme EcoR1, was separated by agarose gel electrophoresis, followed by extraction from the gel. This was then used to create a vector which expresses a fusion protein with the bacterial protein anthranilate synthetase. A relevant fragment in the exact open reading frame was cloned into pATH plasmid vectors (Koerner et al., *Meth. Enzymol.* 194: 477 (1991)). Induction of protein expression was obtained after transformation of the plasmids into E. coli of strain BL21 as described (Spindleret al., *J. Virol.* 49: 132 (1984)). Expressed fusion proteins were separated by SDS gel electrophoresis, excised from the gel, eluted and freeze dried. Rabbits were immunized by subcutaneous injection with 100 µg of the lyophilisate combined with Freund's adjuvant according to standard procedures. Immunization was repeated three times at two-week intervals using incomplete Freund's adjuvant. The rabbit was bled and antiserum was obtained. The obtained antiserum was depleted from antibodies reactive with E. coli and phages as described above and tested for reactivity against the renal carcinoma antigen as described for the human serum.

Reactivity was detected at dilutions of 1: >100,000.

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Additional clones were identified from pancreatic cancer tumor specimen using the SEREX method of Sahin et al., (1995). A cDNA library was prepared and reacted with high titer IgG in sera of pancreatic carcinoma patients. A total of 8x10<sup>5</sup> clones were screened with autologous serum, and 4.5x10<sup>3</sup> clones were screened with three different allogeneic sera. Twenty three clones, representing seven different transcripts were found. Four were previously unknown, unisolated genes. Of the remaining three, glycolytic enzyme aldolase A was found (SEQ ID Nos:799 and 800). Another molecule was "known" in that it was homologous to the rat eIF-5 gene (SEQ ID Nos:801 and 802), which is a eukaryotic translation initiation factor. The human eIF-5 gene was not previously known.

When hepatocelullar carcinoma libraries were studied in the same way, a total of 1.5x10<sup>6</sup> clones were screened, and 98 positives were found. A total of 59 of these were sequenced, and corresponded to at least 20 different transcripts. Nine of these were assayed with allogeneic sera from hepatocellular cancer (HCC) patients and normal patients. High titered antibody was restricted to HCC patients. The majority of isolated sequences did not correspond to known molecules. Three which did were human albumin (SEQ ID Nos:803 and 804), senescence marker protein SMP30 (SEQ ID NOs:805 and 806), and C3VS (SEQ ID NOs:807 and 808). The latter was overexpressed in 2 of 4 hepatocarcinoma tissues, as compared to normal. Expression of SMP30 was found to vary highly.

The methodology was combined with subtractive cDNA techniques when assaying leukemia cells (T-ALL). An antigen was found which was identical to a broadly expressed, DNA repair enzyme.

Further assays identified the known molecule galectin-9 (SEQ ID NOs:809 and 810), as being highly expressed on human macrophages and dendritic cells. Expression is upregulated during differentiation of monocytes to macrophages. Highest levels were found on monocyte derived, dendritic cells.

Fusion proteins "LD1-mFc" and "LD2-mFc" were constructed to help analyze galectin-9. These consist of murine IgG heavy chain fragments, and a lectin domain (LD1, or LD2), as the N-terminus. Analysis indicated that the C-terminal lectin domain binds to the surface ligands, while the cell surface ligands recognized by the C-terminal lectin domain of galactin-9 was expressed only in a small, subpopulation of dendritic cells.

Further analysis of ovarian cancer cells (500,000 clones, using the SEREX method described

above), identified previously known antigens MAGE-4 (SEQ ID Nos:811 and 812) and restin (SEQ ID Nos:813 and 814), and six other newly identified molecules.

Further experiments were carried out which involved restin. A variation of restin is known, i.e., "CLIP170", which was reported to mediate binding of endosomes to microlubules. It was found that both resin and CLIP 170 are highly expressed in dendritic cells, and are involved in the formation and transport of macropinosomes, a feature of professional antigen presenting cells. Expression of restin was induced after 48 hours of culture of monocytes in GM-CSF/IL-4 supplemented medium. Highest levels were found in immature dendritic cells. When microlubile systems, which are essential for the activity of restin/CLIP-170 were disrupted, macropinocytosis was lost completely.

Further work with the methodology disclosed herein on glioma identified a clone encoding nm23-H2 protein (SEQ ID Nos:815 and 816). This clone corresponds to subunit B of nucleoside diphosphate kinase, which is implicated in tumor metastasis control. It is also known as PuF, a transcriptional factor, for c-myc proto-oncogenes. Antibodies against the protein were found in 1 of 18 sera of brain malignancy patients, 3 of 20 melanoma patients, and 2 of 20 sera from healthy patients. When expression studies were carried out using RT-PCR, 25 of 28 brain tumor, and 4 or 5 mengioma tumor samples were found to express the gene.

## Example 9:Isolation and analysis of lung cancer clones

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A cDNA library was constructed from a case of moderately differentiated adenocarcinoma of the lung, obtained from the Department of Pathology at The New York Hospital. The library was constructed in a  $\lambda$ ZAP Express vector using a cDNA library kit (Stratagene, La Jolla, CA).

The cDNA library was screened with autologous patient's serum as described previously [Sahin, U. et al., *Proc Natl Acad Sci USA* 92:11810-3 (1995); Chen, Y.T. et al. *Proc Natl Acad Sci USA*. 94:1914-8 (1997)]. Briefly, the serum was diluted 1:10, pre-absorbed with transfected *E. coli* lysate, and a 1:10 dilution of the absorbed serum (final dilution of serum 1:100) was incubated overnight at room temperature with the nitrocellulose membranes containing the phage plaques. After washing, the filters were incubated with alkaline phosphatase-conjugated goat anti-human Fc γ secondary antibodies and the reactive phage plaques were visualized by incubating with 5-bromo-4-chloro-3-indolyl-phosphate and nitroblue tetrazolium. Phagemid clones encoding human

immunoglobulin sequences were subsequently eliminated during the secondary screening.

The reactive clones were subcloned, purified, and *in vitro* excised to pBK-CMV plasmid forms (Stratagene). Plasmid DNA was prepared using Wizard Miniprep DNA Purification System (Promega, Madison, WI). The inserted DNA was evaluated by EcoRI-XbaI restriction mapping, and clones representing different cDNA inserts were sequenced. The sequencing reactions were performed by DNA Services at Cornell University (Ithaca, NY) using ABI PRISM (Perkin Elmer) automated sequencers.

To evaluate the mRNA expression pattern of the cloned cDNA in normal and malignant tissues, gene-specific oligonucleotide primers for PCR were designed to amplify cDNA segments of 300-400bp in length, with the estimated primer melting temperature in the range of 65-70°C. All primers were commercially synthesized (Operon Technologies, Alameda, CA). RT-PCR were performed using 35 amplification cycles in a thermal cycler (Perkin Elmer) at an annealing temperature of 60°C.

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Genomic DNA were extracted from cell lines and frozen tumor tissue. Following restriction enzyme digestion, the DNA was separated on a 0.7% agarose gel, blotted onto nitrocellulose filters, and hybridized to an a <sup>32</sup>P-labeled DNA probe at high stringency (65°C, aqueous buffer). Washing of the blot was also under high stringency conditions, with a final wash in 0.2XSSC with 0.2% SDS at 65°C.

To identify the 5'end of the mRNA transcripts, RACE (rapid amplification of cDNA ends) methodology was utilized using the Marathon cDNA amplification kit (Clontech) and adaptor-ligated testicular cDNA as the substrate. The PCR products, after separation by agarose gel electrophoresis, were cloned into the direct PCR cloning vector pGEM-T (Promega).

Single-strand conformation polymorphism (SSCP) analysis was performed to analyze cDNA from various tissues, using previously described protocols [Dracopoli, C.D. et al., New York: John Wiley and Sons, Inc. (1997)]. Briefly, PCR was performed with 5  $\mu$ l RT product in a final volume of 25  $\mu$ l, with 2 $\mu$ Ci of  $\alpha^{32}$ P-dCTP (~3000 Ci/mmole, New England Nuclear) per reaction. The PCR conditions was as described for RT-PCR above. After the PCR, 1  $\mu$ l of the mixture was diluted with 5  $\mu$ l of denaturing buffer (95% formamide, 20 mM EDTA, 0.05% bromophenol blue, 0.05% xylene cyanol), heat-denatured at 98°C for 2 min, and electrophoresed through an 8% polyacrylamide gel with 10% glycerol. As controls, aliquots of the same samples were diluted with a standard non-

denaturing DNA loading dye and electrophoresed in parallel. The electrophoresis was performed at room temperature at a constant power of 10-12 watts. The gel was then dried and autoradiography performed for 15-24 hours with an intensifying screen.

## 5 Identification of Immunoreactive cDNA clones

A cDNA expression library of 1.42x10<sup>7</sup> primary clones was prepared from Lu15, a specimen of moderately differentiated adenocarcinoma of the lung and 8x10<sup>5</sup> phage plaques were immunoscreened with absorbed autologous patient serum at 1:100 dilution. Excluding false-positive clones encoding immunoglobulin gene fragments, 20 positive clones were identified. These clones were purified and sequence analyzed. Comparisons of the sequences showed that these clones represented cDNAs from 12 distinct genes, designated NY-LU-1 through NY-LU-12 (Table 9). A homology search through the GenBank/EMBO databases revealed that 4 of the 12 genes corresponded to previously known molecules, and 8 others were unknown genes, with sequence identity limited only to short segments of known genes or to expressed sequence tags (ESTs).

Table 9: NY-LU clones

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Gene Designation	Gene/Sequence Identity [Accession Number]	cDNA	Comments
NY-LU-1	Aldolase A (N and H type) [X06352]	Lu-15/24, 72, 83, 158, 219, 241	Human fructose, 1,6 diphosphate aldolase A.  Expressed in muscle (M type), but also in most other tissues (N and H types). Levels increased in most lung cancers; released into blood upon trauma and in several cancers.
NY-LU-2	hASNA-1 [U60276]	Lu-15/26, 66	Human homolog of the ATP-biding ars A component of the bacterial arsenite transporter.  Previously cloned by SEREX from a testicular library (Chen et al., unpolished). Ubiquitously expressed.
NY-LU-3	Annexin 1X [L19605]	LU-15/64	Homosapiens 56K autoantigen. Antibodies to Annexin 1X are found in multiple autoimmune diseases. ubiquitously expressed.

NY-LU-4	Rip-1	Lu-15/65	Human HIV Rev-interacting protein. Expressed
	[U55766]		in B cells, monocytes and rhabdomyoma cells.
NY-LU-5	Unknown	Lu-15/80	Expressed ubiquitously (by RT-PCR).
	[W61291, W92962, etc.]		
NY-LU-6	Unknown	Lu-15/85	Sequence contains no ORF, expressed
	[none]		ubiquitously (by RT-PCR).
NY-LU-7	Unknown	Lu-	Expressed in neuron, pregnant uterus, lung ca.,
	[W23466, AA167732,	15/135,217	parathyroid tumors, etc.
	etc.]		
NY-LU-8	Unknown	Lu-15/139	Expressed in fetal heart, retin, multiple sclerosis,
	[Z78323, N39225, etc.]		etc.
NY-LU-9	Unknown	Lu-15/145	Expressed in retina, pregnant uterus, fetal liver-
	[W26569, AA036884,		spleen, etc.
	etc.]		
NY-LU-10	Unknown	Lu-15/154	Expressed in colon, pancreas, pregnant uterus,
	[M29204, etc.]		fibroblasts, etc.
NY-LU-11	Unknown	Lu-15/270	Expressed in retina, pregnant uterus, fetal heart,
	[W23466, AA057400,		fetal liver-spleen, parathyroid tumors, etc.
	etc.]		
NY-LU-12	g16	Lu-15/251	Located at the 3p21 TSG locus (see text)

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Of the 4 known genes, aldolase A (NY-LU-1; SEQ ID NOs:689 and 690) was most frequently isolated, representing 6 of 20 primary positive clones in the entire screening. NY-LU-2 (SEQ ID NO:691), represented by two isolates, was the human homolog of the ATP-binding arsA component of the bacterial arsenite transporter, a gene which has been shown to be ubiquitously expressed in various tissues [Kurdi-Haidar, B. et al., *Genomics* 36:486-91 (1996)]. NY-LU-3 (SEQ ID Nos:692 and 693) encodes annexin XI, which is a 56KD ubiquitously expressed antigen to which autoantibodies have been described in sera from patients with various autoimmune diseases [Misaki, Y. et al., *J Biol Chem* 269:4240-6 (1994); Misaki, Y. et al., *J Rheumatol*. 22:97-102 (1995)]. The last gene in this group, NY-LU-4 (SEQ ID NOs:694 and 695), codes for the human HIV Rev interacting protein Rip-1, which has been shown to be expressed in the monocyte cell line U937, the rhabdomyoma cell line RD, as well as in adherent monocytes and primary lymphocytes [Refaeli, Y.

et al., Proc Natl Acad Sci USA 92:3621-5 (1995)].

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Of the eight unknown genes, 6 (NY-LU-5, 7, 8, 9, 10, 11; SEQ ID Nos:696, 698, 699, 700, 701 and 702/703, respectively) shared sequence identify with reported expressed sequence tags (EST), likely representing cDNA products derived from the same genes. These ESTs were derived from various somatic tissues unrelated to lung, e.g., neuron, pregnant uterus, colon, endothelial cells, etc., suggesting that these genes are widely expressed in human tissues (Table 9), making them unlikely candidates for vaccine-based tumor immunotherapy. These clones were not further investigated. The only novel gene in this group, NY-LU-6 (SEQ ID NO:697), showed no sequence identity to deposited sequences in the public databases. The tissue expression pattern of this gene was evaluated by RT-PCR analysis using gene-specific primers and a normal tissue RNA panel consisting of lung, colon, kidney, liver, brain and testis. Results showed universal expression in these tissues, and this clone was not further analyzed.

## NY-LU-12 is on TSG locus of chromosome 3p21.

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The last gene in the unknown gene group, NY-LU-12, was represented by the immunoreactive clone Lu15-251. This clone, 1081bp in length, contained an uninterrupted open reading frame (ORF) of 952 bp, followed by a 129bp 3'untranslated region. No translation initiation codon was identified, indicating that this was a partial cDNA clone.

A sequence homology search revealed that this gene shared up to 30% homology with two different human proteins at its C-terminus (Fig. 1), LUCA15 and DXS8237E (GenBank accession numbers U23946, and P98175) and also shared homology to S1-1, the rat counterpart of DXS8237E [Inoue, A. et al., *Nucleic Acids Res.* 24:2990-7 (1996)]. LUCA15 was subsequently proven to be a gene immediately centromeric to NY-LU-12 on the *TSG* locus on chromosome 3p21 (see below and [Wei, M.H. et al., *Cancer Res.* 56: 2487-92 (1996))]. Our analysis of LUCA15 revealed the presence of a nuclear localization signal in the putative LUCA15 protein. DXS8237E, was located on chromosome Xp11.23 [Coleman, M.P. et al., *Genomics* 31:135-8 (1996)] and its rat homolog, S1-1, has been shown to be an RNA-binding protein [Inoue, A. et al., *Nucleic Acids Res.* 24:2990-7 (1996)].

Of particular interest, however, was that a short segment (92bp) at the 5' end of NY-LU-12 was identical to a previously identified gene, g16 (GenBank accession number U50839), which was

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mapped to chromosome 3p21.3 and was interrupted in the small cell lung cancer line NCI-H740.

To compare NY-LU-12 with g16, the full-length NY-LU-12 cDNA sequence was obtained from normal testicular mRNA through a combination of 5'RACE and direct PCR cloning strategies. The predominant cDNA form (SEQ ID No:707), excluding the poly A tail, is of 3591bp in length. An open-reading-frame of 1123 amino acid residues (SEQ ID No:708) was identified (nt. 102-3470), with 101bp of 5' untranslated and 129bp of the 3' untranslated region. The nucleotide and amino acid sequences are shown in Fig. 2.

Comparison with the g16 sequence verified that these two are identical genes and mapped NY-LU-12 to TSG locus on 3p21. However, the reported g16 sequence, 2433 bp in length, lacks the 5' end 110 bases which include the translational initiation codon at nucleotide 102, and also the 3' end 980 nucleotides of NY-LU-12. In addition, 74bp DNA segment (nt. 1587-1659 of NY-LU-12) was absent in the reported g16 sequence. Oligonucleotide primers flanking this 74 bp region were designed and used to amplify RNA from 1 normal lung, 5 lung cancer cell lines, and 6 lung cancer specimens. Two RT-PCR products were seen in every specimen, corresponding to the sizes of the two cDNA variants. It was thus concluded that this variation represents an alternate splicing event which occurs in both normal and cancerous lung tissues. Of interest, however, was the difference in the putative translational products resulting from this additional 74bp exon. In the absence of this exon, the open-reading-frame of NY-LU-12 would end in the termination codon at nt.1736, as reported for g16, with a total length of 520 amino acid residues (in contrast to 1123 residues in the longer transcript). Moreover, this shorter form would not encode the C-terminal portion of the NY-LU-12 protein, the segment responsible for the immunoreactivity of Lu15-251 to the autologous patient serum.

## Additional cDNA variants of NY-LU-12

In the process of 5'RACE cloning of the full-length NY-LU-12, three minor forms of cDNA products were identified which varied in their transcriptional initiation site and in their exon usage in the 5' segment of this gene. These variants will be described as transcripts B, C, and D (SEQ ID Nos:709, 711 and 712). Fig. 3 shows the comparison of these transcripts to the predominant cDNA form (transcript A, see Fig. 2).

Transcript B (Fig. 3A, bottom) contains an additional exon of 208 base pairs, inserted at

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nucleotide 145 of the NY-LU-12 sequence. The original ORF of NY-LU-12 is disrupted due to this inserted sequence, and the AUG initiation codon used by transcript A is thus unlikely to be used by this transcript. A new potential translational initiation site, however, is found within this new exon and would continue the translation into the ORF of transcript A. The final product would be a protein of 1177 amino acids (SEQ ID NO:710), with the 69 residues at the N-terminus different from transcript A. Interestingly, this new exon encodes for a signal peptide not present in the transcript A (Fig. 3A, bottom), and it is possible that these two products are localized to different subcellular compartments.

Similar to transcript B, transcripts C and D both contained additional exon(s) not present in transcript A. Transcript C contained two extra exons in tandem and a length of 364bp, only one of which (137bp) was present in transcript D, Figure 3B. These extra exon(s), inserted at the same alternate splicing site as transcript B, disrupted the original ORF, and the only long ORF would initiate at nucleotide position 498 of NY-LU-12 (959 of transcript C, 635 of transcript D). Considering the long untranslated region at the 5' end, it is doubtful whether transcripts C and D are indeed translated *in vivo*.

Correlating with this variation of NY-LU-12 mRNA, Northern blot analysis showed several RNA species in normal tissues, ranging approximately from 3 to 4.4 Kb. The intensity of individual bands also appear to vary among different tissues, suggesting post-transcriptional tissue specific regulation of NY-LU-12 mRNA.

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# Features of NY-LU-12 and its putative gene product

Analysis of the NY-LU-12 amino acid sequence showed 20 inexact 6 amino acid repeats with a consensus sequence of D(F/Y)RGR(D/E) close to the N-terminus (Fig. 2). These repeats were separated by 4 to 6 amino acid intervals, which showed no apparent sequence homology among each other. This feature in primary sequence is distinctive among known proteins. Hydrophilicity plot revealed that this region, although hydrophilic in general, has regular hydrophobic turns, and these cycles of hydrophilicity changes correspond to the hexapeptide repeats. Although the significance of this characteristic is unclear at present, this segment of sequence is highly rich in arginine and aspartic acid, a feature shared by RNA binding proteins. Similar motifs, rich in arginine and aspartic acid residues, were found in other RNA-binding proteins [Witte, M.M.

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et al., *Proc Natl Acad Sci USA* 94: 1212-7 (1997); Wilson, R. et al., *Nature* 368:32-8 (1994); Seraphin, B. et al., *Nature* 337:84-7 (1989); Takagaki, Y. et al., *Proc Natl Acad Sci USA* 89:1403-7 (1992)], e.g., RNA [Seraphin, B. et al., *Nature* 337:84-7 (1989)] hnRNA 3'end cleavage stimulation factor [Takagaki, Y. et al., *Proc Natl Acad Sci USA* 89:1403-7 (1992)], etc., indicating that NY-LU-12 is likely to be an RNA-binding protein. Consistent with this, PROSITE analysis of the putative NY-LU-12 protein identified a bipartite nuclear localization signal between amino acids 1016-1032 and a 4-residue nuclear localization pattern (PRKR) at amino acid 604-607 (Fig. 2), suggesting that NY-LU-12 is a nuclear protein. Analysis for post-translational modification sites showed potential sites for tyrosine sulfation, amidation, as well as phosphorylation sites for protein kinase A, C, casein kinase II, and tyrosine kinase. A PEST region, peptide sequences consistently found among unstable proteins with short half lives, was identified at amino acids 897-928 (Fig. 2), implying NY-LU-12 as an unstable protein.

### Southern blot analysis of NY-LU-12 in normal and tumor tissues

To investigate the status of NY-LU-12 in normal and tumor cells, Southern blot analysis was performed on 9 lung cancer cell lines (3 adenocarcinoma, 2 squamous, and 3 large cell anaplastic), Lu15 tumor DNA, and a colon cancer cell line HT29 (Fig. 4). (HT29 was included due to the finding of an EST identified in the GenBank, accession number AA079461, which appeared to be a fusion sequence between semaphorin IV gene and NY-LU-12.) Using a 1.1Kb cDNA probe (nucleotide 1095-2140) and HindIII digested DNA, the results showed that one of the two hybridizing bands was absent in NCI-H740, confirming that NY-LU-12 was partially deleted in this cell line. The breakpoint of this deletion, by using primers from different regions, was further defined to be between nucleotides 1433 and 1777 of NY-LU-12, with the 3' sequences homozygously deleted. Besides NCI-H740, however, no evidence of homozygous deletion was seen in any other tumor cell line sample or in LU15. The similar band intensities and identical sizes of the DNA signals in all specimens also argued against the possibility of a heterozygous deletion or translocation of this gene, at least in the region analyzed. No change was found in HT29, suggesting that the semaphorin IV/NY-LU-12 fusion sequence in the GenBank probably represents a cloning artifact.

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## SSCP and sequence analysis of NY-LU-12 in Lu15 tumor DNA.

The mapping of NY-LU-12 to the lung cancer *TSG* locus raised the possibility that an altered protein product due to mutational event may be the basis for the autologous immune recognition. This possibility was explored using DNA sequencing and single-strand confirmational polymorphism (SSCP) analysis.

The DNA sequence contained in the immunoreactive clone Lu15-251 (nucleotide 2518-3599 of NY-LU-12) was obtained from the normal counterpart by RT-PCR cloning using autologous normal lung tissue, and no mutations were found when compared to Lu15-251.

RT-PCR SSCP was then used to analyze the entire NY-LU-12 gene, comparing Lu15 tumor tissue and autologous normal lung tissue. To encompass the whole sequence, 10 sets of primer pairs were designed, each amplifying a range of 205 to 603 bps. For products >400bps, a restriction enzyme digestion step was added prior to the electrophoresis step to further reduce the fragment sizes and increase the assay sensitivity. Results showed no reproducible changes between normal and tumor tissues, and thus no evidence of mutation in Lu15 tumor cDNA. A representative set of SSCP analysis is shown in Fig. 5.

## Serological response to NY-LU-12 in lung cancer patient

The frequency of anti-NY-LU-12 response was examined among normal adult and patient sera using the phage plaque assay identical to the original immunoscreening procedure. Of 21 absorbed sera from allogeneic lung cancer patients, one (Lu22) reacted strongly with the Lu15-251 plaque at 1:1000 dilution, and another (Lu7) also reacted at 1:1000, but only weakly. Nineteen other lung cancer patient sera were non-reactive, nor were the sera from 16 healthy donors, 15 colon cancer, 5 breast cancer, 1 renal cancer, 1 prostate cancer, 1 esophageal cancer, and 1 melanoma patients.

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## Example 10: Expression analysis of additional cancer associated nucleic acids

The clone RING 3 was isolated from breast SEREX analysis as LONY-Br-5 (see above). The gene was identified as homologous to the "bromodomain testis" gene (BRDT; GenBank accession number AF019085). Analysis of related genes identified BRDT as a gene expressed only in testis, which was then investigated by RT-PCR analysis as described above.

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The primers used to perform RT-PCR had the following sequences:

BRDT F1: CAAGAAAGGCACTCAACAG (bp 543-563 of BRDT)

BRDT R1: TTCACTACTTGCTTTAACTGC (bp 776-797 of BRDT)

The meiotic protein H1T (Histone 1 Testis; GenBank accession number M60094) was

5 identified through a literature search for meiotic proteins (testis specific expression).

The primers used to perform RT-PCR had the following sequences:

H1F1: TGCCGAACCTCTCTGTGTC (bp 116-135 of H1T)

H1R1: GCTTCGTGTAGATTTAGGAATC (bp 344-366 of H1T)

## Table 10: RT-PCR analysis

	Normal Tissue	BRDT	<u>H1T</u>
	mammary gland	-	-
	liver	-	-
15	small intestine	-	-
	brain	-	+/- (very weak)
	lung	-	-
	fetal brain	-	-
	placenta	+	+
20	kidney	-	-
	skeletal muscle	-	-
	pancreas	-	-
	adrenal gland	-	-
	heart	-	-
25	thymus	-	-
	uterus	-	-
	prostate	-	+/- (very weak)
	spleen	-	-
	Testis	+	+
30		*	
	Tumor Tissue	BRDT	HIT
	Colon	0/6	0/6
35	Breast	0/6	6/6+
	Melanoma	0/12	3/12+
	Lung	8/26+	4/26+
	Renal	0/2	0/2
	Ovary	0/2	0/2
40	Esophageal	0/1	0/1

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Gastric 0/1 0/1 Bladder 0/2 0/2

Lung cancer specific expression of BRDT was observed (see table above). BRDT was expressed only in normal testis and possibly in placenta. The expression analysis of H1T revealed that all breast tumor samples (6 of 6) and ~30% lung cancers and melanoma tissue samples expressed H1T. H1T was expressed in normal testis and possibly in placenta and brain.

## Example 11: allogeneic serotyping

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To confirm the cancer associated expression of SEREX clones, allogenic sera screening of gastric cancer patients' sera was conducted. Sera from normal patients (gastritis) was used as a control for expression of the clones in non-gastric cancer. The screening procedure used was as described above for the SEREX screening, except for the absorption of anti-bacterial and anti-bacteriophage antibodies. The modifications were as follows.

Serum from a stomach cancer patient or a normal individual was diluted to 1:10 in TBS (Tris buffered saline; final volume 5 ml) and passed through a column (BIO-RAD Poly-Prep Chromatography Column, Hercules. CA, USA) containing 0.5 ml Sepharose-4B cross linked to E. coli Y1090 lysate and 0.5 ml Sepharose-4B cross linked to E. coli BNN97 (5 Prime 3 Prime, Inc, Boulder, CO, USA). After repeating the column chromatography 10 times, serum was then diluted to 1:100 in TBS containing 1% BSA and 0.02% sodium azide. To remove antibodies to bacteria and baceteriophages further, 10 ml absorbed serum was incubated overnight with a 82 mm nitrocellulose membrane on which XL-1 Blue MRF' bacteria and lambda ZAP Express phages (Stratagene, La Jolla, CA USA) were immobilized. The serum was stored at - 80°C until use. For allogeneic typing, an equal numbers of positive phage and negative phage were mixed and plated and processed by the standard SEREX screening procedure.

The results of the allogenic screening experiments follow:

Table 11: Allogenic Sera Screening of SEREX Sequences from Gastric Patients

	Sequence		Isolated	Allogenic Serotyping	Allogenic Serotyping
	Gene/Clone	Number	in Serex Patients	Gastric Cancer Sera	Normal Sera
	RPB-J H-2K binding factor	110111001	SM1	6/12	6/16
5	Telomeric repeat binding protein		SMI ·	1/12	0/16
	Ser/Thr protein kinase		SM1	1/12	0/16
	SRY interacting protein-1		SM1	2/12	1/16
	Sterol carrier protein X		SM1	2/12	0/16
10	Archain		SM1	1/12	1/16
	HEM-1		SM1	2/12	1/16
	Id-1 helix-loop-helix protein		SM1	1/12	0/16
15	helix-loop-helix transcription factor		SM1	1/12	0/16
	Follistatin related precursor protein		SM1,CK, KM	6/12	0/16
	Translation initiation factor eIF-4gamma		SM1,SS1, KM	5/12	2/16
20	M phase phophoprotein I		SM1,SS1	8/12	5/16
	Lysal tRNA synthase		SM1	1/12	0/16
	Gelsolin		SM1	4/12	0/16
	Zinc finger protein		SM1	1/12	1/16
	Goliath		SM1	2/12	1/16
25	zhx-1		SM1	1/12	1/16
	SG24		SM1,SS1, KM	5/12	0/16
	SG132		SM1	3/12	0/16
	S553		SM1	7/12	7/16
	S134		SM1	3/12	0/16
30	S328		SM1	2/12	1/16
	S365		SM1, KM	2/12	0/16

Γ	FKBP25	KM, SS1	5/12	0/16
	Pros-27	KM, CK	3/12	1/16
	BS4	KM	1/12	1/16
	GnRH-II	KM	1/12	0/16
5	СТВР	КМ	1/12	0/16
	ETF	KM	3/12	1/16
	KIAA0438	KM	1/12	5/16
	KIAA0367	KM	4/12	3/16
Ī	APK1	KM	2/12	0/16
10	IPP	КМ	1/12	. 0/16
	Tropomyosin	КМ	1/12	0/16
	p63	КМ	1/12	0/16
	KIAA0181	КМ	1/12	0/16
T	KIAA0349	КМ	1/12	0/16
15	RPB1	КМ	5/12	9/15
ľ	PPIM	КМ	1/12	•
	EB virus	КМ	3/12	-
-	G.KM073	КМ	6/12	-
Ī	G.KM403	КМ	1/12	-
20	KM192	KM	. 1/12	-
Ī	KM294	КМ	1/12	-
	KM362	КМ	1/12	-
	KM031	KM	1/12	-
	KM081	КМ	3/12	-
25	KM201	KM	1/12	-
Ī	KM1496	KM	1/12	•
Ţ	KM334	KM	1/12	
	KM313	KM	1/12	
Ì	E-cad/Y	СК	1/12	0/16
30	IPBP	SSI	1/4	-
İ	OS-9	SS1	1/4	-

Kinesin light chain	SS1	1/4	-
<u> </u>			

The screening results shown above confirm the association of the SEREX clones with cancer. There is a higher correlation of cancer and the expression of certain clones, in particular, follistatin related precursor protein, the translation initiation factor eIF-4gamma, the unknown sequence SG24, the FK506-binding protein 25, and the unknown sequence G.KM073. These clones are well suited to serve as diagnostic indicators of disease and as targets for therapeutics (e.g., vaccine compositions) development.

# 10 Example 12: Preparation of recombinant cancer associated antigens

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To facilitate screening of patients' sera for antibodies reactive with cancer associated antigens, for example by ELISA, recombinant proteins are prepared according to standard procedures. In one method, the clones encoding cancer associated antigens are subcloned into a baculovirus expression vector, and the recombinant expression vectors are introduced into appropriate insect cells. Baculovirus/insect cloning systems are preferred because post-translational modifications are carried out in the insect cells. Another preferred eukaryotic system is the *Drosophila* Expression System from Invitrogen. Clones which express high amounts of the recombinant protein are selected and used to produce the recombinant proteins. The recombinant proteins are tested for antibody recognition using serum from the patient which was used to isolated the particular clone, or in the case of cancer associated antigens recognized by allogeneic sera, e.g. certain breast cancer and gastric cancer associated antigens, by the sera from any of the patients used to isolate the clones or sera which recognize the clones' gene products.

Alternatively, the cancer associated antigen clones are inserted into a prokaryotic expression vector for production of recombinant proteins in bacteria. Other systems, including yeast expression systems and mammalian cell culture systems also can be used.

## Example 13: Preparation of antibodies to cancer associated antigens

The recombinant cancer associated antigens produced as in Example 12 above are used to generate polyclonal antisera and monoclonal antibodies according to standard procedures. The antisera and antibodies so produced are tested for correct recognition of the cancer associated

antigens by using the antisera/antibodies in assays of cell extracts of patients known to express the particular cancer associated antigen (e.g. an ELISA assay). These antibodies can be used for experimental purposes (e.g. localization of the cancer associated antigens, immunoprecipitations, Western blots, etc.) as well as diagnostic purposes (e.g., testing extracts of tissue biopsies, testing for the presence of cancer associated antigens).

# Example 14: Expression of cancer associated antigens in cancers of similar and different origin.

The expression of one or more of the cancer associated antigens is tested in a range of tumor samples to determine which, if any, other malignancies should be diagnosed and/or treated by the methods described herein. Tumor cell lines and tumor samples are tested for cancer associated antigen expression, preferably by RT-PCR according to standard procedures. Northern blots also are used to test the expression of the cancer associated antigens. Antibody based assays, such as ELISA and western blot, also can be used to determine protein expression. A preferred method of testing expression of cancer associated antigens (in other cancers and in additional same type cancer patients) is allogeneic serotyping using a modified SEREX protocol (as described above for gastric clones).

In all of the foregoing, extracts from the tumors of patients who provided sera for the initial isolation of the cancer associated antigens are used as positive controls. The cells containing recombinant expression vectors described in the Examples above also can be used as positive controls.

The results generated from the foregoing experiments provide panels of multiple cancer associated nucleic acids and/or polypeptides for use in diagnostic (e.g. determining the existence of cancer, determining the prognosis of a patient undergoing therapy, etc.) and therapeutic methods (e.g., vaccine composition, etc.).

## Example 15: HLA typing of patients positive for cancer associated antigen

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To determine which HLA molecules present peptides derived from the cancer associated antigens, cells of the patients which express the cancer associated antigens are HLA typed. Peripheral blood lymphocytes are taken from the patient and typed for HLA class I or class II, as

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well as for the particular subtype of class I or class II. Tumor biopsy samples also can be used for typing. HLA typing can be carried out by any of the standard methods in the art of clinical immunology, such as by recognition by specific monoclonal antibodies, or by HLA allele-specific PCR (e.g. as described in WO97/31126).

5

# Example 16: Characterization of breast cancer associated antigen peptides presented by MHC class I and class II molecules.

Antigens which provoke an antibody response in a subject may also provoke a cell-mediated immune response. Cells process proteins into peptides for presentation on MHC class I or class II molecules on the cell surface for immune surveillance. Peptides presented by certain MHC/HLA molecules generally conform to motifs. These motifs are known in some cases, and can be used to screen the breast cancer associated antigens for the presence of potential class I and/or class II peptides. Summaries of class I and class II motifs have been published (e.g., Rammensee et al., Immunogenetics 41:178-228, 1995). Based on the results of experiments such as those described in Example 15, the HLA types which present the individual breast cancer associated antigens are known. Motifs of peptides presented by these HLA molecules thus are preferentially searched.

One also can search for class I and class II motifs using computer algorithms. For example, computer programs for predicting potential CTL epitopes based on known class I motifs has been described (*see*, *e.g.*, Parker et al, *J. Immunol*. 152:163, 1994; D'Amaro et al., *Human Immunol*. 43:13-18, 1995; Drijfhout et al., *Human Immunol*. 43:1-12, 1995). HLA binding predictions can conveniently be made using an algorithm available via the Internet on the National Institutes of Health World Wide Web site at URL http://bimas.dcrt.nih.gov. Methods for determining HLA class II peptides and making substitutions thereto are also known (e.g. Strominger and Wucherpfennig (PCT/US96/03182)).

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The lung cancer SEREX clone polypeptides NY-LU-12 and NY-LU-12B (variant B), SEQ ID NOs: 708 and 710, were subjected to the HLA binding peptide analysis described above, using the NIH website, to identify HLA binding peptides for several common HLA molecules (HLA-A1, A2, A3, A24, B7, B44, and B52). The results are listed below in Table 12.

Table 12: Identification of HLA binding peptides in lung SEREX clones

## amino acids of

	<u>HLA</u>	<u>peptide</u>	NY-LU-12 protein	SEQ ID NO
	A1	NVEE-HSFSY	67 - 75	713
		PVDP-NILDY	287 - 295	714
5		DTDY-RSMEY	398 - 406	715
	<b>A</b> 2	SLLE-DAIGC	506 - 514	716
		TLMI-QDKEV	521 - 529	717
		YVSSLDFWYC	533 - 542	718
10		VIVEVLEPYV	671 - 680	719
		KLTD-WNKLA	948 - 956	720
		QLSDLHKQNL	975 - 984	721
		KQSEQELAYL	991 - 1000	722
		KLVDKEDIDT	1042 ~ 1051	723
15		VMFA-RYKEL	1114 - 1122	724
	<b>A</b> 3	QMFG-YGQSK	417 - 425	725
		GMPVKNLQLK	481 - 490	726
		GLPE-EEEIK	823 - 831	727
20		LLCRRQFPNK	958 - 967	728
	A24	EYRD-VDHRL	405 - 413	729
		GYVC-VEFSL	499 - 507	730
		DYGY-VCVEF	497 - 505	731
25		WYCKRCKANI	540 - 549	732
		TYPQPQKTSI	574 - 583	733
		IYRSTPPEVI	663 - 672	734
		HYYQ-GKKYF	754 - 762	735
		VYVP-QDPGL	816 - 824	736
30				
	B7	WNRDYPPPPL	26 - 35	737
		MPPV-DPNIL	285 - 293	738
		TARD-AQRDL	432 - 440	739
		GPSEEKPSRL	448 - 457	740
35		TPPEVIVEVL	667 - 676	741
		RVMFARYKEL	1113 - 1122	742
	B44	REMG-SCMEF	272 - 280	743
		EEQSSDAGLF	376 - 385	744
40		KEYN-TGYDY	490 - 498	745
		TEAKQELITY	566 - 575	746
		VEALRVVKIL	710 - 719	747
		GEYG-GDSDY	906 - 914	748
		LERREREGKF	1000 - 1009	749

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	B52		650 - 659	750
		TPPEVIVEVL	667 - 676	751
		YGFIDLDSHV	701 - 710	752
_		RQFP-NKEVL	962 - 970	753
5				
	NY-L	U-12B (variant	: В)	
	A1	NVEE-HSFSY	121 - 129	754
10		PVDP-NILDY	341 - 349	755
		DTDY-RSMEY	452 - 460	756
	A2	WQSA-RFYYL	41 - 49	757
		SLLE-DAIGC	560 - 568	758
15		TLMI-QDKEV	575 - 583	759
			587 - 596	760
		VIVEVLEPYV	725 - 734	761
		KLTD-WNKLA	1002 - 1010	762
		QLSDLHKQNL	1029 - 1038	763
20		KQSEQELAYL	1045 - 1054	764
		KLVDKEDIDT	1096 - 1105	765
		VMFA-RYKEL	1168 - 1176	766
	A3	QMFG-YGQSK	471 - 479	767
25		GMPVKNLQLK	535 - 544	768
		GLPE-EEEIK	877 - 885	769
		LLCRRQFPNK	1012 - 1021	770
	A24	YYLN-ATDVL	47 - 55	771
30		FYYLNATDVL	46 - 55	772
		EYRD-VDHRL	459 - 467	773
		GYVC-VEFSL	553 - 561	774
		DYGY-VCVEF	551 - 559	775
		WYCKRCKANI	594 - 603	776
35		TYPQPQKTSI	628 - 637	777
		IYRSTPPEVI	717 - 726	778
		HYYQ-GKKYF	808 - 816	779
		VYVP-QDPGL	870 - 878	780
40	מים	MIDDVDDDI	0.0	201
40	В7	WNRDYPPPPL	80 - 89	781
		MPPV-DPNIL	339 - 347	782
		TARD-AQRDL GPSEEKPSRL	486 - 494	783
			502 - 511	784
45		TPPEVIVEVL	721 - 730	785
43		RVMFARYKEL	1167 - 1176	786

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	B44	SEAWSSNEKF	59 - 68	787
		REMG-SCMEF	326 - 334	788
		EEQSSDAGLF	430 - 439	789
		KEYN-TGYDY	544 - 552	790
5		TEAKQELITY	620 - 629	791
		VEALRVVKIL	764 - 773	792
		GEYG-GDSDY	960 - 968	793
		LERREREGKF	1054 - 1063	794
10	B52	RQDGESKTIM	704 - 713	795
		TPPEVIVEVL	721 - 730	796
		YGFIDLDSHV	755 - 764	797
		RQFP-NKEVL	1016 - 1024	798

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Likewise, other clones identified herein can be analyzed for the presence of candidate HLA binding peptides using no more than routine experimentation.

# Example 17: Identification of the portion of a cancer associated polypeptide encoding an antigen

To determine if the cancer associated antigens isolated as described above can provoke a cytolytic T lymphocyte response, the following method is performed. CTL clones are generated by stimulating the peripheral blood lymphocytes (PBLs) of a patient with autologous normal cells transfected with one of the clones encoding a cancer associated antigen polypeptide or with irradiated PBLs loaded with synthetic peptides corresponding to the putative protein and matching the consensus for the appropriate HLA class I molecule (as described above) to localize an antigenic peptide within the cancer associated antigen clone (see, e.g., Knuth et al., Proc. Natl. Acad. Sci. USA 81:3511-3515, 1984; van der Bruggen et al., Eur. J. Immunol.24:3038-3043, 1994). These CTL clones are screened for specificity against COS cells transfected with the cancer associated antigen clone and autologous HLA alleles as described by Brichard et al. (Eur. J. Immunol. 26:224-230, 1996). CTL recognition of a cancer associated antigen is determined by measuring release of TNF from the cytolytic T lymphocyte or by <sup>51</sup>Cr release assay (Herin et al., Int. J. Cancer 39:390-396, 1987). If a CTL clone specifically recognizes a transfected COS cell, then shorter fragments of the cancer associated antigen clone transfected in that COS cell are tested to identify the region of the gene that encodes the peptide. Fragments of the cancer associated antigen clone are prepared by

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exonuclease III digestion or other standard molecular biology methods. Synthetic peptides are prepared to confirm the exact sequence of the antigen.

Optionally, shorter fragments of cancer associated antigen cDNAs are generated by PCR. Shorter fragments are used to provoke TNF release or <sup>51</sup>Cr release as above.

Synthetic peptides corresponding to portions of the shortest fragment of the cancer associated antigen clone which provokes TNF release are prepared. Progressively shorter peptides are synthesized to determine the optimal cancer associated antigen tumor rejection antigen peptides for a given HLA molecule.

A similar method is performed to determine if the cancer associated antigen contains one or more HLA class II peptides recognized by CTLs. One can search the sequence of the cancer associated antigen polypeptides for HLA class II motifs as described above. In contrast to class I peptides, class II peptides are presented by a limited number of cell types. Thus for these experiments, dendritic cells or B cell clones which express HLA class II molecules preferably are used.

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## **EQUIVALENTS**

Those skilled in the art will recognize, or be able to ascertain using no more than routine experimentation, many equivalents to the specific embodiments of the invention described herein. Such equivalents are intended to be encompassed by the following claims.

All references disclosed herein are incorporated by reference in their entirety.

We claim:

#### TABLE 1

## SEQ ID NO. 1:

5 U72994, AC004022, Z68323, AE001160, L34078, AF064863, AC002132, U60440, X66494, N21242, AA678312, W86762, R01605, AA782843, AA275156, W41927, AA874648, AA571241, AA562747, W10480, AA451301, AA866631, AA466667, AA999057, AI029140.

#### 10 SEQ ID NO. 2:

AC004022, U72994, AC002420, AC004125, AA690961, W41927, AA874648, AC004022, U72994, AC002420, AC004125, AA690961, W41927, AA874648.

SEQ ID NO. 3:

X98371, AL009008, L31790, Z83220, X92946, AC003975, AF008916, U80460, X75544, X66732, X95275, X52177, X07976, AC004451, Z74307, AB000878, AL009179, AF038667, Z78544, Z48008, U23486, J05096, AB000882, Z30213, L11593, U18530, L27325, AC005191, M99579, AA130270, AA158245, AA903098, AI018453, AA436455, AA980593, AA172479, AA637487, AA116588, AA426854, AA050404, AA390025, AI006618, AI048382, C85944, AA673480, AI006510, AA823338, AA413694, W35075, AA015033, AA413584, W29693, AA637069, AA619839, AA125149, AA039004, AA674696, AA871138, AA414747, AA198099, C91478, F071359, AA925957, AA820054, H16496, AI043756, AA892435, AA893551, AA818669, AA892785, AA944026, D33919, N96570, F19798, AI045451, AA800662, D65187, AA944025, AA925731, AA892314, AA945449.

#### 30 SEQ ID NO. 4:

AA900930, AA925665.

## 35 SEQ ID NO. 5:

U58105, Z81485, Z54236, Z48584, U61375, M55267, M59856, X51942, U77302, Z48621, AF032455, Z11866, AB013392, L32792, AA871997, AA084083, AA130829, AA083063, AA666290, N38894, D54459, T28921, AA806015, AA512059, AI043087, AI042894, AA968324, AA238493, AA237462, AI042885, AI046424, AI035670, AA269430, AA250621, AI035540, AA260613, AA106870, AA238658, AA106134, AI042683, AA105958, AA144007, AA986558, AA457910, AA389400, AA673056, AA153254, AA754678, AI021109, AA390813, C36687, T41571, AI011183, AI013356, AI011739, AI030260, AA924384, C44421.

SEQ ID NO. 6:

45

AF036717, U91327, AF036718, U56248, Z48795, Z99290, M30697, U58204, M24417, AF022983, M33581, AC004619, H64641, AA477478, AA369676, AA088359, AA057574,

AA683066, AA446279, AA332363, T09328, R80982, AA069486, AA410842, C18527, AA293033, H12730, AA287344, AA029631, R83063, AA061290, AA185993, AA880204, AA499308, AA183172, AA242360, AA792388, AA175587, AA277140, AA880395, AA899046, AA859550, C35363, C35702, C32682, F14140, T18049, C83149, T45787, AA924623, D47525, Z30723, AA897884, AA042465, AI009871, AA875198, C83016.

## SEQ ID NO. 7:

X74116, AL022148, AC004548, AC000352, Z11664, Z78065, Z74028, AE000163, AE000750, X74229, D90700, R59414, AA176708, W02568, AA354664, R43017, AA973553, F10008, D61827, AA826300, Z41398, T77572, R40189, H85823, W86541, T17276, AA679337, X83357, AA184845, AA416260, AA475603, AA388692, AA764445, AA388689, AA219880, AA290020, AA388507, AA387267, C86741, AA414436, AA451259, AA413796, AA930916, AA793690, AA619447, AA062257, AA522026, AA816247, AA892032, AA817702, H33461, AA925507, AA849449, AI029236, AA247069, AA697975, AA882508, AA893258, AA698410, AA891755, AA698227, AA892782, AA899328, T04373, AA567522, AA698408, AA202615, AA141016, AA697974, AA697998, C61176, D69691, AI030205, AA586054.

## SEQ ID NO. 8:

20

U08218, L38909, Y11095, AC002431, Z23069, S77418, U39060, L38580, AF053367, Z36506, M18102, J03624, AA102264, AA730686, H47968, AA357170, AA130974, C06054,
SA626429, F00559, AA604528, AA383348, AA040127, N84965, D54884, D54883, R94309, AA373184, AA128091, W68194, H58283, R76347, AA343938, AA305144, AI049611, AA384516, AA720553, N57395, R97387, D52674, AA169408, H66293, AA456362, T74258, AA730145, AA101952, N86388, AA355003, AA307640, AA385679, AA354542, N99075, N83528, H87678, R84494, R35720, AA670111, AA186452, W32370, D55392, W05161, AA641280, AA120503, C77063, AA146393, AA620177, AA509478, C77481, AA427148, AA474531, W83304, AA207424, AA763436, AA958473, AA799243, AA493061, AA967792, AA145256, AA089338, AA756259, AA789767, AA980112, AA866640, AA914516, AA821675, AA466770, AA015387, AA816036, AA246546, AA941789, AA955779, AA997768, AA997534, T43805, AA956150, T18836, T23333, AA525666, T18787, AA800483, C64685, AA851367, C91730, AA143899, T23399.

## SEQ ID NO. 9:

AP000056, U43491, Z74919, L81498, Z94054, AC002503, L81499, AA740188, AA630241, AA974724, AA806907, N88859, N98242, H12649, R06485, R06511, AA546258, C76846, AA208416, AA959219, AA276381, W10055, AA462844, AA444278, W13447, W97802, AA542324, AA137880, AA269331, AA175695, W59029, AA003372, AA146233, AI045761, C93154, C94084, C94208, D68027, C12780, AA687005, AA080598, C12876, C12390, AA848674, AA924440, T15031, AA451569, H35524.

#### SEQ ID NO. 10:

U25640, AA127328, H24207, H08275, AA283063, AA826096, AA417382, AA464874, W05562, AA453370, N51211, AA495859, R33871, H00927, AA623997, AA220442, AA178568, AA605493, AA394557, AA956116, AA999037, AA818246.

5 SEQ ID NO. 11:

AB001740, AF039956, AA581972, AA594539, AA236870, AA464410, AA237069, AA694199, AI038896, AA167314, AA577381, AA430117, N23143, R53610, W37647, AA724229, AA313202, AA860618, W16866, AA134966, AA2555556, AA305224, R50528, AA844913, W32042, W37383, AA908394, W93357, W31353, R55254, N79251, AA456077, AA477700, AA477701, AA989005, AA455580, N32722, N22935, R50622, AA135047, R51941, T34020, T30416, T32309, AA883332, W93445, AA166984, AA026749, T08224, AA255572, W03768, AA033670, W31880, AA772832, AA230974, AA511207, W82274, AA230365, AA671085, AA511230, AA606681, AA023735, AA444535, W98518, W14718, W85455, AA980318, AA137525, AA035840, AA692158, AA007919, W48013, AA444534, AA981497, AA002566, W48089, W99869, AA960396, AA960580, AA145259, AA145683, AA388960, AA389941, AA266272, AA145124, AA267212, AA959753, AA407991, A175818, AA943997, AA899476, AA899756, AA943998, AA955446, AA012783, AA924956, AA892219, AA955331, AI012225, AA891436.

#### SEQ ID NO. 12:

U72994, AC004022, AF043493, U43252, U43251, U81830, U58105, U68242, Z93242, AL009029, M29872, U12980, M81118, M30471, Z56258, AF012943, AC004080, AC002563, AF024533, AF002991, Z63771, AP000042, AF064863, U80017, AC004087, Z55235, L05920, AA508139, N90748, AA450240, AA948158, AA828938, AA165115, AI003312, AA436633, AA419100, AA743442, AA961990, AA885286, AA861312, T84801, AI040166, AA494115, AA652324, AA181105, AA095541, R59256, AA503712, AA700364, AA603821, T60326, AA779097, AI023884, AA603785, H79111, W39526, AA506607, W94361, N66078, R01605, H22694, W86762, W99303, AA745640, AA678312, AA431870, W41927, AA874648, C92734, C23102, C53080, C91168, D65098, C32959, C50029, M80125, C34452, C83862, C24659, T21473, AA874720, C06696, W43071, AI043300, C53907.

### SEQ ID NO. 13:

35

X94232, U90437, AC003052, U59809, AC004001, M95396, Z67884, X77486, U70051,
X14805, AF022976, Z83823, X77485, J04171, AF036007, U05768, U88315, Z98048,
AF036009, AC005179, U41277, U32517, AE001138, D64060, M84387, H29022, AA814221,
N26314, AA935912, AA873506, AA608576, AA453605, AA232674, Z38725, AA772022,
AA025212, AA318330, R48115, AA234084, H18508, N64543, AA970508, R36933,
AA306944, H49559, AA325555, H85834, H89988, AA343974, AA648643, H65664, T62713,
H16554, N21122, AA351037, AA484621, AA221492, AA259314, C76383, C76336,
AA607924, C76394, AA408562, AA921258, AI006352, W41405, AA153317, AA015435,
AA027405, AA794066, AA498038, AA184222, AI011068, AA859614, AA899776, AA955080,
AA799674, AA849652, AI009788, AA900928, AI007950, AA109392, AA753592, U92780,
AA957632, AA567950, AI009495.

## SEQ ID NO. 14:

AC000075, U66140, R14195, AA220229, T31199, R19104, R19148, Z46126, AA417619, Z45284, H14105, R84666, AA090321, AA350108, W52840, R48497, R13097, T66255, W44467, AA247676, AA198489, AA388175, AA261453, AA237111, AA790730, AA162394, AA816498, AI013729, AA684961, AA979759.

#### 10 SEQ ID NO. 15:

AF069301, D10651, U11419, U11287, M91562, U90278, U72724, X57855, X79424, M16512, M64542, Z14152, AF016667, L01488, Z75955, AF024504, M13968, W67775, AA934587, AA617696, AA913577, AA628682, W74527, AA969876, AA995606, AA622402, AA027090, AA620556, AA085733, AA187157, AI031865, AA972318, AA897169, W79046, AA531124, AA733183, T90909, Z25096, AA721771, AA115089, T49643, R00622, N93780, R00626, AA365494, T71475, N74066, AA027130, T83325, AA115569, AA658299, T55344, T83700, AA426250, AA393863, AA282967, R08138, AI000112, AA807574, AA077926, AA397527, W87761, AA243026, R56368, H16371, AA958697, AA003997, AA008542, AA036229, AA397074, AA250467, AA260498, AA968175, AA253686, AA727785, AI019478, AA474978, AA543461, AA990281, AA245791, AA617042, AA015355, AA983015, AA982200, AA120064, AA462778, AA242574, AA986993, AA986911, AA882490, AA223057, AA543989, W65528, AA848318, AA874979, AA800547, AA945302, AA140994, AA991110, AA851120.

## SEQ ID NO. 16:

25

Z68106, X14199, M14872, Z63497, M31670, AC002123, Z63498, AA280070, AA215687, H93207, AA070367, W95534, AA682436, AA741066, AA173269, AA641255, AA215688, AA724798, N23259, AA442155, AA634563, AA074699, AA642322, AA861347, AA283655, AI002587, W95419, AA357042, AA761253, AA197191, T54480, AA133029, AA378991, AA114599, AA219925, AA174327, AA003800, C86661, AA990433, AA277014, AA445101, AA671205, AI036728, AA241221, AA213304, AI035350, W08919, W36663, AA061406, AA144736, AA240583, AI006563, AA980152, AA250075, AA088967, W17488, AA098269, W10200, AA543712, AA755434, AI012680, AA820868, AA949519, AA391130, AA202576, AA979150, AA012391, AA539472.

## 40 SEQ ID NO. 17:

J03592, M24103, AB009386, U44832, J02966, M24102, U27316, U10404, X70847, D12771, D12770, J02683, J03591, U27315, M76669, U39779, M13783, J04982, X74510, X61667, M57424, L78810, AC004000, Z75206, U68723, Z75207, AF009661, X53264, J03320, U66060, AB011800, M77194, AE000021, L07268, AE000936, U03115, AF009663, AA582128, AA916851, AA576667, AA915921, AA916853, N58735, AA428106, AA427849, AI024255, H69807, H11315, N36980, H69597, AA826334, W05080, N37044, AA385873, N48222, AA394173, AA837522, AI002511, AA292870, T96300, AA360716, AA379604, AA862844, AA430455, AA479859, AA133899, AA669954, H92542, AA095298, AA995794, AI003667,

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## SEQ ID NO. 18:

U14003, AE000500, X66784, AF030178, U77066, M10122, M69106, X58072, Z99113, AF004104, AF004101, X55037, X78560, AC004595, X55122, AA481578, AA280143, AA481271, AA280144, AA736516, N79995, R82883, AA355987, AA571000, AA572293, AA738653, AA620225, AA855746, AA563168, AA530645, W40812, AA690944, AA839456, X61848, AA525648, AA141861, AA944854, C94212, AA394778, C83861, H76642, AA559379, AA943112.

## SEQ ID NO. 19:

AE000500, AF030178, X66784, Z49405, M69106, M27174, X55037, AF004104, X78560, U51281, L17405, M10122, AC003106, X55122, X05553, AC002368, AF004101, U77066, U77456, X58072, AA481578, AA280143, AA481271, AA280144, AA736516, AA780050, AA359089, R82883, AA355987, AA571000, AA563168, AA738653, AA620225, AA855746, AA572293, AA530645, W40812, AA690944, AA839456, X61848, AA525648, AA944854,

AA141861, C83861, AA943112, AA957703, H76642, C94212, AA394778.

## SEQ ID NO. 20:

5 Z99496, AC004518, AC004219, Z70204, J03925, Z66494, AC003053, U40072, AC002980, S52165, AB009051, M81884, AL021767, Z68164, M18044, J04145, AA383216, AA928132, Z19212, R84841, H83829, T71075, AA723804, H95329, AJ003438, W13441, AA199243, AA242009, AA272568, AA009230, AA880181, AA265864, AA124746, AA801108, AA874804.

## SEQ ID NO. 21:

U20864, AL021246, AA430998, AA050776, AA104086, AA414390, AA920944, AA624117, AA788028, H36635.

#### SEQ ID NO. 22:

Z81462, AF029308, AC004069, AL010265, AL023828, AC004026, AF076274, U96110,
Z71181, AF000265, U59919, Z80108, X66974, Y15994, D50366, D50367, AA034417,
AA053882, AA883340, AA132258, AA770253, AA132362, AA132257, T62545, AA425357,
AA721474, AA483037, AA724043, AA491390, W27229, AA047351, AA247867, C01523,
AA548452, AA024660, R53754, AA795672, AA199329, AA986113, C81340, AA914941,
AA536730, AA819693, Z28994, AA142165, AA585560, Z26382.

#### SEQ ID NO. 23:

30 X60469, AC000394, L08048, X12597, D63874, U51677, S71186, D43920, U59897, AF026132, AB012725, L02751, D88509, M15825, AF017349, AB002361, L49022, Z82196, S68108, AC005266, M60450, M55514, AC004406, AF019611, AC000398, U28932, AF049850, X58671, AC004101, AC004687, AF062921, AF004294, M33190, M73049, U00665, L04132, AF039845, L06147, M60052, X56007, Y00500, X77934, U26708, AL022333, AL021710, AF005720, Y13901, AC003952, U02506, U61387, AC004491, M81784, U00763, M80414, U84223, X87461, AF006040, U82468, AF005900, U29175, D26156, L13025, AL021127, X87329, Z82076, U25126, M30298, M34041, S80994, L13856, J03806, U23805, U20951, D82352, M38742, U05192, D76432, M21683, U19460, L48363, D78647, U26259, M55017, L06098, L19713, U88047, S67316, U47276, U28389, U18650, M85183, U07886, U00762, X54504, S67319, M89788, AC002995, AC000370, D84418, Z46757, AA167070, AA595202, AA166712, C05079, AA632468, T64162, H14432, AA095130, AA304799, AA541691, W38700, AA593710, AA889358, AA079129, T64291, AA143566, AA481443, AA991543, AA404267, H92212, AA134178, AA991539, AA991535, AA134179, AA248062, AA079130, AA634670, D25983, H63841, AI025061, AA531274, AA366296, AA360842, F22618, AA366810, N88386, AA715713, T90564, N38949, AA045606, W07682, D55472, AA557452, AA600212, H89557, AA327933, D20752, AA083771, AA101746, AA563764, AA330028, AA987424, AA054783, D83849, R34185, D52874, R81133, D55190, AI034040, N26696, AA196344, AI041775, AA054719, M79245, H54611, AA813685, R43019, AA426205.

AA527046, R10011, R14525, AA053848, H85928, N85207, AA536117, AA497040. AA017619, AA093385, F08518, T70173, N83954, W28966, H98185, AA506305, R07822, T05370, AA652934, AA021126, AA236110, R93864, AA643226, N52274, AA046288, AA079860, H80808, R54825, W28236, AA537503, AA288865, AA914010, AA546178, AA895780, AA921471, AA509592, AI019685, AA792002, AA821727, AA466161, AA122542, AA387328, AA172425, C87724, AA895923, AA259495, W18813, AA960471, C87940, AA921284, Z74659, AA407850, AA675676, AA738607, AA619874, Z74640, AA881206, W97542, AA896321, AA106515, AA562363, AA797955, AA895398, AA123213, AA798375, AA467444, AA123743, AA611503, AA388279, AA516863, AA588982, AA169099, AA727617, AA516854, AA560832, AA793428, AA120232, C80564, C81382, AA412789, AA607305, AA039151, AA415500, AA529643, AA080345, AA238459, C80723, AA467433, AA473693, C77886, C80539, AA915029, AI037742, W58796, AA591350, AA623692, AA792889, W91681, AA051589, AA060808, AA116289, AA267544, AA444983, AA498517, AA590755, AI021142, AA114557, AA270502, AA790432, C85885, AA123204, AA170036, AA211953, AA438133, W79965, AA591380, AA624294, AA624917, AA386884, AA636994, AA386974, AA469668, AA795177, AI050523, C94974, C83593, C82737, N37420, C92269, H35981, AA818062, C73802, AA720311, D41136, F15112, D46038, AI035042, C83610, AA875659, D41283, C82754, H36775, H32221, D41870, AA860020, C25027, AA224679, AI008510, L46426, C08715, C28364, AA684640, AA941159, D22112, AA264452, D15403, H34930, D40666, D41146, AA750433, C20172, C74114, AA800271, C91616, D23315, AA800199, C27928, C73183, AA801317, AA955860, AA801633, D42374, AI043271, AA816245, AA439680, AA605835, AA540843, D40984, Z71869, AA979311, C70650, AI012063, AA392031, U94861, D15662, C08297, C11108, C11146, C31764, C34637, C37817, C47184, C52269, C54739, C58131, C58618, C36053, AA898501, AA951524, T01370, D40028, D48397, D72544, D72553, AA963561, M89319, D24210, D23745, D72761, C59680, AA820741, T01827, D42962, AI035194.

## SEQ ID NO. 24:

30 Z93928, U13881, U70475, X89811, X81456, U20532, X04724, J00748, M25585, J04807. V01243, M12913, AC003074, AE000626, AA662803, AA886335, AA922036, AA878578, AA161103, AA485405, N52768, AA643750, AA910277, N52783, AA657904, AA631339, AA158820, AA485566, N57590, N57604, AA127055, T25136, C21312, N50304, AA127056, C01240, W65459, AA416662, N48671, AA759070, N29058, H06159, R97183, F20369, W74006, AA210618, AA825287, T15787, R67195, T91328, H06144, AA608823, W74282, T52487, R17253, T50700, AA710096, AA793203, AA106190, AA674919, AA691210, AA709564, AA688482, AA709549, AA286083, AA637633, AA863920, C86279, AA940262, AA675156, AA986540, AI006503, C78301, AA413934, W33763, AI035505, AI036707, AA498683, AI046409, C85159, Z84147, AA893230, C06683, C06682, C06639, C06625. C06581, AI029119, C06813, C06751, C07055, C06613, C06863, C06604, C07135, C07117, C07030, C06535, C07018, C06636, C06511, C06605, C06612, C07058, C06908, C07105, C06559, C06724, AI014020, C07031, C06541, C06767, C06618, C06546, C06906, T75705, C06519, C06802, C06669, C06655, C06560, C07009, C06616, C06506, C06510, C06652, C06750, C06806, C06950, C06971, C06974, C06608, C06788, C06890, C06536, C06778, C06831, C07167, C06840, C06946, C06513, C06642, C06914, C07148, C06600, C06925, C07008, AA851621, C06514, C07107, C09614, C06525, H31786, C06858.

## SEQ ID NO. 25:

AF019412, AC004404, X06166, M65066, AF006040, R13835, Z43662, F07559, R87914, AA323632, AA806551, AA351660, AA404545, AA693604, T77601, AI039071, AI017031, AA489394, AA664956, W73671, AA057240, AA129710, AA342548, T93900, W73623, N53667, AA725874, AA804595, AA907520, W56587, H68702, AA323997, T64725, AA884894, AI022045, R02181, AA279068, T19926, AA733025, W51682, AA822148, AA138982, AA267343, AA709923, AA423781, AA185617, AI006077, W82491, AA062192, AA270251, W54396, AA718043, AA451528, AA387186, AA388304, AI021006, AA458323, AA734717, C72433, AA940925, T26042, AA998047, AA651398, AA712850, AA979380, AA851912.

#### SEQ ID NO. 26:

15

D38548, M59201, U67559, L29453, L27707, X52142, M58326, U49350, AL021806, AA323338, AA287807, AA378829, AA826533, AA524104, AA928732, AA127169, AA515984, AA962233, AA332628, W90207, W55983, R98570, AA937512, AA190722, AA409809, AA027693, W15854, W82920, W14373, AA624765, AA958909.

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## SEQ ID NO. 27:

AJ005458, S90449, S74572, D17412, D17411, U09218, D45860, D45861, D45859, S87759, S87757, AJ005457, J04503, D28117, AL009051, AL022603, M86359, Z84489, AA625572, AA431963, AA180531, AA180520, AA379401, AA164383, AA135096, AA769851, AA465249, Z19798, Z20951, AA625571, AA854244, AA625051, AA193078, X85622, N88139, AA179618, R33159, R79167, AA613881, AI042584, N83569, AA360057, AA011060, AA154560, AA276352, W54488, W54415, C87503, AA549511, C85223, W08528, AA656770, AA497692, AA855719, C85235, AA407160, AA516930, AA240636, W41595, AA475660, AA914011, AA537063, W42402, AA033036, AA644993, AA517242, C85347, AA525713, AA962971, AA998206, AA394677, AA998046, Z71861, H31577, C19204, AI045015, R65006.

## 35 SEQ ID NO. 28:

Z84812, X56744, AB007445, AE000947, AF038854, X98801, AB013487, U40575, AF002992, D79209, U33840, U55042, AF000168, U76615, L28716, U31977, L25548, L23646, AF037987, AF037988, AF037986, X16944, AF037455, X61920, AB004061, U21050, K00824, Z47005, U02478, L00627, Z74150, M35657, AF037984, X15477, AA070233, AA768890, AA704738, AA491544, AA747198, AF012388, AA453482, AA393092, AA351249, F08069, AA576778, C18739, W02878, AA260806, AA792752, AI037115, AA107079, AA606798, AA267705, AA833235, C79173, C79128, C78861, AA655446, AA254466, AA674661, AA212535, AA008734, AA879626, W41067, AA619200, AA087347, AA138013, AA547261, AA002419, AI021096, AA275231, AA433044, AA221284, AA822351, AA014416, AA986428, AA221500, W64585, AA739293, AA450489, AA616218, AA673749, W09948, W80148, AA058081, AA111583, AA109879, AA516815, AA759685, AI047206, AA036090, AA475741, AI044800, W00180, AA997260, AA439137, AA996688, AA964874, AA750540, AA749776, C36210, R03414, AA520514, AA519480, T01878, AI026368, AA531657, H77262, T01090, N38684,

AA965082, R46894, T37779, T37753, T38689, C24841, AA519236, T38077, N60531, C56520, C39038.

## 5 SEQ ID NO. 29:

M37030, AF035811, AF073312, X61452, AF061152, AF006988, U59632, AF061153, Y11593, U74628, U08103, Z98866, Z69710, U52918, U52919, D89208, AA262134, AA262133, AA459232, AA261944, AA465590, AA480946, AA252838, AI003777, AA322577, W05228, AA323006, AA451780, T09445, R55858, AA324456, R87202, F11317, T30876, AA322117, AA357101, AA853747, AA325651, AA683394, W69297, H46499, AA055270, AA350932, H14250, AA024634, AA234283, L44408, AA604064, N55150, AA462547, AA146273, AA789450, AA873999, AA791509, W64849, W85596, AA444524, AA572240, AA032529, AA469889, R75180, W53226, AA020101, AA762779, AA869090, R74897, AA238408, AA867045, AA415500, C78795, W54807, AA266548, AA511393, R74879, F14565, C57606, C57776, C59287, AA539919, D35810, C65610, D36489, D34951, AA950835, C66232, AI012506, C62041, D37043, C67579, AA696662, C60241, C13766, C69199, AA685788, D66025, D66320, D66176, AA550227, D66297, C57131, C58693, D65593, AA800156, D65694, C64990, D69331, D65426, D68791, D66117, D66340, D66241, C12616, D66000, H76149, D65431, H34478, D69657, D65625, M89459, AA819212, D69682, D70222, D65711, D65685, D69823.

## SEQ ID NO. 30:

AL022394, Z54200, U12024, AF025391, S73606, L08068, U01053, AP000046, AA282633, H83341, AA744757, AA047741, AA975917, W45279, W90155, W79733, H01158, N47513, AA688093, AA865203, W90027, AA595381, AA054203, AA478596, AA100549, T80668, AI049820, AA047691, AA969720, AA086374, AA159414, W39756, AA159315, H83695, AA909221, T06258, AA969838, AA013361, H05751, H05858, AA665540, D12197, H01159, AA933811, D12219, AA282525, C05204, N47512, R57383, F18424, D79284, W92778, H18813, H20386, N77238, R84635, AA204675, R80129, W95005, T85150, AA523436, AA743656, T84782, W95004, R55724, AA572180, AA790119, W96964, AA420091, AA169954, AA623914, AA623971, AA681631, H32698, AA735717, AF026318.

## SEQ ID NO. 31:

35

X17644, AC002310, U95742, L37045, Z92835, L38828, L07843, X56910, AF025468, X62379, X53599, X73911, X57331, U25851, AC004217, AA488455, AA112360, AA085969, W39758, AA450255, AA385764, AA306361, F08788, AA133458, AA331334, AA357236, N83925, AA319543, AA907882, AA295194, AA780612, AA805179, AA091629, AA233394, T52577, AA352655, AA211401, AA223759, AA187286, T51341, R66786, H17719, T08767, AA865254, AA761172, AA219613, AA169748, AA761180, AA878125, M62053, H97773, AA775004, N47792, AA580452, N77885, H20947, R39533, R16161, AA916422, AA446700, AA918094, AA960808, AA873720, H84809, F10962, D78656, AA917945, AA404653, W67540, AA430019, AA643603, AA603207, AA446573, AI014813, AA988575, C14668, R15819, AA769334, AI041235, R46057, W19901, W55959, H60522, AA219635, AA133573, AA406042, AA670040, AI022461, AI005124, AA931798, AA918010, AA904626, AA708261,

AA721503, AA279498, R46796, R12508, Z40330, AA455678, AA054518, N36991, AA879059, AA683027, AI026067, AA669953, AA088745, W55958, AA396956, AA555800, AA154170, AA981643, AA071792, AA066012, AA981626, AA154214, W14994, AA197464, AA109909, AA260252, AA416413, AA389313, AA204468, AA109518, C77638, C77886, AA183642, AA415277, AA987053, AA138979, AA145942, AA666768, AA795476, AA197732, AA815895, AA106800, AA657049, AA096871, AA671011, AA062392, AA474044, W46023, AA959293, W35880, AA516832, D67123, AA495624, C74197, D68097, C24919, D65118, X73715, R30624, AA586106, AA819013, W43432, AA799892, AA858586, AA142059, T44911, C92734, AA952406, AA495523, AI030315, AA676129.

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## SEQ ID NO. 32:

AF017364, D78609, AF011331, AJ223316, X69524, AF019907, AF009411, AF009413. U44430, AF069324, AF001501, AF009959, M99575, Z54362, U60149, AF029349, AJ005572, Z28367, Z97178, D83476, U62398, AF001688, U50847, AF022732, AF045770, AF019887, AF006628, L41731, AF026216, U74296, AF016371, AF006627, AF020187, AB002739, AB002741, AJ225108, S80963, U19482, D83352, AB002728, U38894, AF001522, U46118, AB002794, U82480, AB002730, U10355, AJ005969, AF022733, Y15794, U14936, AF019043, S51033, U58090, AB002777, X71980, AB015609, U25846, U55848, Y14339, AB002533. U43527, U48288, AF004947, L10111, U35364, AF058796, U08214, AF023132, Y11879. Y13865, U33214, U41060, AF048691, AB005545, M69042, U37699, U40802, Y09455, X77990, U64609, AF071010, L49502, AD000017, S68736, M82977, AA121558, AA927567, H92975, R67157, AA039781, AA078892, AA454159, AA354002, AA934648, AA356829, H58224, AA316922, AA977788, H78570, AA953223, AA992339, U30151, H48430, D82132. D57213, C75478, C18748, C75472, C75170, D82799, AA362857, AA374918, C75020, Z28355, AA357303, C05952, AA301748, D63057, D82421, C75176, AA669404, C05853, AI016032, C16591, D59976, C75108, D57346, C75118, C19093, L48852, T27986, U30155, D62770, AA317816, AA365617, D52369, T110921, C06140, AA357401, N93837, D51124. N75780, C18589, AA083604, AA471140, AA354268, C06018, Z21605, L48853, H90908, AA188141, D57197, AA573490, AA587755, AA070452, AA302374, AA303144, AA352846, AA374865, AA976510, T69957, D60150, D80615, N71594, C05868, C14789, AA355029, H73203, AA113291, AA303336, AA358041, AA301756, D59695, T27384, C18745, AA308574, AA271637, AA549023, W85152, U31322, AA106372, AA795651, AA457999, AA681967, W49394, AA221922, AA276547, AA242387, AA061250, AA146431, AA021897, AA596536, AA183239, AA271248, AA389067, AA871189, AA145354, W09313, AA030290. AA871865, AA124414, AA052617, AA871752, AA544610, AA117188, AA869120, AI049175, AA266008, W98973, C76233, W66614, AA199206, AA221363, AA254150, AA268605, AA867829, AA185301, W12393, AA073318, AA174921, AA212810, AA254516, AA387162. AA596462, C77430, AA986671, AA062512, AA388966, AA555783, AA177472, AA106040, AA553155, W30212, AA286196, W12857, AA717172, AA065453, AA267923, AA242444, AA396448, AA217994, AA111828, AJ005971, AA123661, AA114501, AA752812, R47079, AA754144, AA509249, AA509214, AA754103, AA840962, AA840909, AA754200, AA509237, W51718, AA753300, AA509309, AA842677, AA752086, AA754036, AA753093, AA754159, AA754172, AA754167, AA751994, AA751845, AA751998, AA752003, AA751816, AA752422, AA751932, AA751561, AA753150, AA754119, AA840970. AA752005, AA842862, AA752043, AA752907, AA752718, AA752020, AA840977, AA752035, AA752016, AA753086, AA109333, AA701820, AA752034, AA547916, AA840986, AA547812, AA841367, AA751857, AA406980, AA471673, AA842464,

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## SEQ ID NO. 33:

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U10079, U22176, Z97192, X86553, D16432, Z68908, X98417, X97752, AC005176, AC004235, AA211771, AA019927, AA621920, R49915, AA436746, D81089, F07201, AA279576, R61642, AA363761, N90952, AA351423, W85802, AA827923, N41673, AA452942, AA252094, W95240, AA188552, T99151, T53177, AA223851, AA677535, AA770162, W85753, H58876, AA017014, W57195, AA117575, W41201, AA415215, AA797940, C76608, D16065, T18290, D16046, AJ225545, AA713066, AJ225477, D22650, AA944738, AA849372, T25220, D23185, D22651, D23309.

#### 20 SEQ ID NO. 34:

AF041845, U48436, AF012624, L76569, AF025020, AF060179, U51281, Z37092, L12249, D83476, AF017434, AF062008, Z97198, AP000046, AA367417, AA852175, W67669, AA303139, AA243251, AA896193, AA881167, AA989888, AA683969, W62376, AA250652, AA512820, AA237481, AI036738, AA547433, W97958, AI036611, AA656921, AA892380, AA926074, D72379.

## SEQ ID NO. 35:

30

AF069301, D17030, D17201, S80107, M15888, U09205, J00127, J00128, M64982, L11356, M58569, AE001140, D10667, M77812, AF001548, U39850, AA188052, W28824, AA380387, AA393863, AA426250, F00243, AA157205, R00525, AA137720, AA244463, AA118832, W97106, AA674322, AA645183, AI020701, AI019310, AA717623, W48327, AA153061, AA103723, AA800548, T46478, AA751512, C10724, C60506, AA819627.

## SEQ ID NO. 36:

40 U81160, U35246, U66865, AF036234, Z71178, R52780, AA336715, AA337057, R12336, AA296712, AA291962, AA336501, AA387806, AI020063, AA109010, AA867718, AA606883, C11880, AA698152, D65730, AA851373, AI028830, AA941242.

## 45 SEQ ID NO. 37:

## **SEQ ID NO. 38:**

Z46933, AC003957, X64346, U18759, L31881, U18761, J04123, X79489, U18760, AB012234, U11280, Z35865, AC002461, AC004780, AL008980, Z79601, U23404, Z74859, D89119, AC000387, M76665, Z48149, AA948725, AA226732, AA232882, AA232883, AA767922, W39443, N40268, W06854, AA337266, AA319281, T08800, AA094683, AA151630, T33776, AA151682, AA384011, R21292, AA806313, AA047744, AA411384, H41338, H49115, H50377, C89065, AA221399, AA163971, Z36313, AA120075, W64578, AA673947, AA285838, AA607874, AA798884, C86947, W62715, AA790168, AI037229, AI036718, AA920062, AA866467, Z30824, AA610965, AA907958, AA495425, W43775, C41467, C20235, C20223, C19643, C20439, C68506, C73712, C20236, AA978809, M89274, D74720, AA712627, D74758, C19867, AA816719.

## SEQ ID NO. 39:

L41560, Z66499, AC003970, AE001177, AF051320, K02212, D88539, U35665, L41069,
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AA046661, AA459381, R77891, R60953, AA733213, W05472, AA442998, AA136770,
AA127983, AA229166, AA741465, AA003716, AA204457, W34842, AA097555, AA674958,
AA770799, W81850, AA623806, C78185, AA002533, AI030850, D26771, AA924818,
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## SEQ ID NO. 40:

AB002307, X06289, Y00222, U59322, U28964, X61754, AJ004801, U13913, X79339, AA164880, R02386, AA219744, AA324396, D82199, AA113090, AA305260, AA171458, R59748, R35620, AA326344, AA227875, AA366276, H29212, AA505691, R78747, AA406622, AA020232, W64555, AA450476, W44167, AA049918, W64627, R75474, AA517492, AA612452, AA711884, AA212469, AI048148, AI046831, AA671392, AA855606, AA016843, AA031134, AA208052, AA619148, W34918, AA851114, AA901667, AA054812, AI001233, AA955131, AA943821, AI008608, C72506, AI001373, AI001376, D25096, D21962, AA997901, AA824936, AA998885, AA824820, AA998125, AA859586.

## **SEQ ID NO. 89:**

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AF069301, D17030, D17201, D10651, U90278, U11287, U11419, M91562, U28411, J00127, J00128, L11356, AE001140, M58569, U72724, M64982, AC002082, AF016667, M80474, X57855, M64542, X79424, Z75955, AF024504, M16512, M13968, M96930, W67775, AA617696, AA934587, AA628682, AA913577, AA969876, W74527, AA995606, AA622402, AA027090, AA426250, AA393863, AA620556, W79046, AA085733, AA187157, AI031865, AA027130, AA115569, AA897169, AA972318, AA365494, AA282967, AA531124, AA733183, T90909, T71475, Z25096, T83700, W28824, AA721771, AA188052, T83325, AA115089, T49643, R00622, R00525, R08138, N93780, R00626, R00521, W67774, N74066, AA157205, AA380460, AA658299, AA380387, T55344, F00243, N55668, AA353778, AA815401, AA399269, AI018748, AA412669, AI028745, AI025290, AI000112, AA813227, AA807574, T61743, T74407, AA397527, AA077926, T60362, AA344542, H67459, T73868, AA026737, T95711, N33594, T72304, W87761, T71715, T72978, T74485, H58121,

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## SEQ ID NO. 91:

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## 30 SEQ ID NO. 93:

AF039700, AF039699, U66201, U66197, AF020738, U85773, Z46966, AC004301, U86662, W22160, AA860926, AA348243, AA551799, AA327309, AA344913, AA121174, AA121198, AA001561, AA040802, AA215903, AA826741, W32428, AA888147, AA403143, AA946650, AA969632, AA872272, AA903406, AA860208, AA577174, AA514777, AA160827, AA041240, W45005, AI005324, AI005204, N72025, AA806381, AA725024, AA262229, AA927863, AA172158, AA039536, R02514, W47466, AA587486, AA629243, AA814296, AA877455, AA435587, AA393904, AA022495, W47341, N35888, N35076, AA974988, N21678, N72024, AI040354, AA804907, AA573297, AA416559, AA401079, AA417295, AA873216, AA824270, AA759038, AA757360, AA628544, AA618498, AA503727, AA460961, AA461270, AA813115, AA759377, AA770473, AA262162, AA416815, R82551, AA948291, AA416734, N98472, AA431486, H30248, AA161105, AA852281, AA616807, AA106439, AA711859, AA049011, AA016868, W61547, AA009071, AA543280, AA467482, AA106301, W83172, AA103139, AA000268, AA014223, AA138067, AA230758, AA833479, AA014768, AA276740, AA038869, AA797372, AA185487, AA881111, AA763419, AA790448, AA469884, W77724, AI048515, AA007762, AA497479, AA033481, AA475425, AI047077, AA068686, AA796056, C87249, AA921560, W87202, AA542324, AA967316. W62989, AA530735, AA218431, AA591243, AI047609, AA692425, AA966976, AA856298. W20935, AA111190, AA230661, AA840087, AA089210, AI035925, AA824205, AA793845,

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## **SEQ ID NO. 95:**

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## **SEQ ID NO. 97:**

AF053974, X96705, U22237, AC004260, Z66517, Z77134, U32723, U35657, AC002080, J04355, U82202, Z35601, K01711, AL022598, M20865, AA374801, AA306449, N48227, H64263, T51666, R52634, AA318276, AA706990, AA551148, AI028232, AA581365, AA694052, W87336, W47503, AA554571, AA607765, AA154690, AA924880, D23509, AA067503.

**SEQ ID NO. 99:** 

Z22176, AL010226, U67566, Z96798, U09956, X56775, Z97339, Z70206, X56260, U67594, AF052832, X52572, Z98598, AC002294, U41554, U66261, M97618, U00149, AC004745, AC004255, Z72888, Z72846, D90759, J03297, M36386, Z65781, U49960, AC003096, AC005238, M20147, AF014960, X07289, M80571, Z71527, Z68277, Z81066, D90852, Z68105, Z99165, U07065, Z92540, AC002432, AC002351, D14533, AL021635, U14566, Y00067, Z73971, U53502, L35848, U10343, U59711, U33934, U28487, M76702, M10066, Z65782, U86962, D85428, U33933, AE000221, AC004135, U62293, X64461, U15591, D90758, AA047345, C75194, AA152132, T39704, AA404974, AA313387, AA377300, AA773368, AA362228, AA047344, AA247511, T40740, W38779, AI050068, R13549, AA346462, N50523, W27312, AA551073, AA306922, AA034218, AA496544, AA975271, AA033534, AA155696, AA423826, AA989046, AA115605, AI024233, AA620978, AI033843, AA115471, AA115213, AA134882, AA559320, AA610042, AA135338, AA248692, R70913. AI022302, AA046587, AA307285, AA781036, AA692567, AA681336, AA549004, AA563487, AA177677, AA915150, AA153059, W41094, AA445202, AA498066, AA409473, AA177599, AA562914, AA266872, AA656061, AA896022, AA117475, AA738723, C77886, X61844, AA674119, AI045314, X91731, C71913, T02509, AA925983, T03973, T02602, AA753121, D48485, AI009917, D24757, D24759, C29123, C28355, AI011347, AA695453, C70381, H36637, C23428, C62223, AA696075, AT000376, AA264575, C63593, AA440992, C48257, AA264245, C23391, AA392990, AA949994, R90723, D47512, C23189, C28792, AA264789, C23091, C23221, C23281, C23486, AA651405, AA791285, L47867, AI030465, W23399, AA802503, C23380.

25 SEQ ID NO. 101:

L41679, AE000664, X70810, M97702, AF007261, AC004052, Z70040, U95973, AB006205, U18340, AC004281, M57977, AF015262, X78823, Z48930, U92453, AF047660, U45982, Z22178, U18338, Z83107, U18337, Z69907, U84551, Z81369, AC004136, U12769, D16355, U06755, AA353592, AI017212, Z20462, AA084913, AA322347, H67555, H15054, R60319, AA782925, AA113206, R41988, H09807, H68176, AA325657, AA635184, W00737, R52825, R44297, Z41301, R34253, AA351933, F05557, AA382460, AA861207, AA688169, AA813930, H97901, AA504297, AA907592, C17555, AA437174, R80561, AA485838, AA287335, AA297740, AA489714, AA722140, AF017648, AA804212, AI015606, AI005291, AA913492, R75960, AA343951, AA334986, AA292286, AA258087, AA025640, R66450, AA843675, AA865754, AA527317, AA232238, N30011, R73028, H27866, H12877, R72656, N69992, AA481805, AA138080, AA615376, AA265134, AA140400, AA608248, AI047363, AA146296, AA930813, AA575341, AA388659, AA462933, AA958463, AA656418, AA589980, AA869843, AA087361, AA792077, AI006571, AI021357, AA690956, AA895651, AA110646, AI046734, AA655927, AA415593, AA200384, AA162290, AA549901, F15585, AA955266, D33207, AA540536, F14406, R03451, AA850731, W06651, D33188, C92137, N97695, D34445, AI029865, AI010659, AA926162, AI045900, AA859190, D32367, AI043939, AI028821.

**SEQ ID NO. 103:** 

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S78798, AF039698, AF045432, U65376, U48696, U39066, L07590, U66300, L12146,

AF033565, U52868, Z97178, S83098, U44386, AF027174, U37573, Z49980, AF033096, AF033097, AJ001103, U34048, G29058, G29060, U41811, X99051, X99055, U48697, D86970. X65215, Z35641, L12469, X80164, Y12256, S56922, AA442655, AA768893, AA779510. AA632212, W88679, T52585, AA132101, N86694, AA093224, N83993, N84718, N55681, N83992, AA471338, AA247827, N56555, N84712, AA093861, N84048, N89520, AA094237, N83991, N84830, AA096066, N88496, N84721, N87989, N88601, AA089553, H58760. AA215911, AA089554, N56118, N83168, N84855, AA247964, N84016, N55698, N88782, AA095641, N84602, N84828, N84733, AA096046, N84723, N87898, N55684, N84561, AA095359, N84874, N85900, AA093897, N88518, N84764, N84722, N55669, N55641. AA249064, AA248551, N84736, AA215908, N55658, N85031, N84873, N84829, N84711, N84734, N84735, N84563, N56179, N84720, N55697, AA090034, AA248055, AA214702, N85930, N84562, N55639, AA247965, N87317, N55653, AA263076, N84601, N86441, AA248540, AA210625, N55717, H54881, AA471140, N84665, N83229, N84714, AA216240, AA285245, N84921, AA095435, N86439, AA093577, N55721, AA247828, W64759, W85389, AA170187, AA017792, AA020604, AA733792, AA208274, AA755285, AA717172, AA866729, AA286214, W10227, AA166319, AA217994, AF041408, AA933116, AA933363. D21922, D22036, W99281, AI010427, AI014137, AA957307, AA866225, AI012477, AI008733, AA996445, AA925786, AA818841, AA924371, AA849942, AA925635, AA999172, AI011706, AA955950, AA963429, AA957899, AI014042, AI010357, AI012277, AA946050, AA997129, AA998014, AA899344, AI009863, AI010298, AA859978, AI045178, AI012192, AA956403, AA998620, AI009737, AA958000, AA859266, AA964570, AA944452, AI013760, AI043606, AI045050, AI010101, R46936, AA900052, AA900076, AI008975, AI045193. AI012602, AA899521, AI009352, AA946359, AI009797, AI009148, N99339, AI030877, AA012039, AA754231, AA817994, AA859429, AA875121, AA900424, AA924214, AA945660, AA964165, AI009800, AA800835, AA858619, AA924931, AA933168, AA945755, AA946378, AA956107, AA957339, AA998987, AI013389, AI043647, AI043787, AI045635, AA660039, AA754049, AA963340, AI007843, AI011499, AI012461, AI044977, AA924075, AI044978, AI045381, AI045262, AA842888, AA901302, AI009757.

## SEQ ID NO. 105:

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U23946, U73168, D50912, U35373, D83948, U50839, AF042857, AF069517, U97008, Z68013, Y08502, U76753, Z28389, AA570533, N23866, AI049957, AA889659, A699426, AA782487, AA767408, N29616, N41616, T03540, AA436772, AA194028, AA724105, AA648939, AA904276, AA907774, AA192891, AA349791, AA677951, AA593262, D19618, AA437179, F09819, AA659891, AA456007, AA165466, AA961715, AA907700, Z40342, R45218, AA975284, AA563802, AA888076, AA670261, T31362, AA150773, AA994080, W73892, W76177, T33106, R45829, R37062, AA421795, R42942, AA337186, AA194215, AA192645. T10051, AA877988, AA150882, AA782825, R60960, AA746150, T10050, AA953465, AA249486, AA369780, AA367141, AA917711, AA165366, AI016061, T32698, AA382385, R21564, N74644, AA383548, AA773506, AA361795, AA359822, R24955, Z19624, AA129882, N31418, AA136550, T50042, AA143444, AA599498, AA374055, AA143443, H19190, R52382, AA761351, AA459583, AA806592, Z43337, R60959, AA890595, H68058, H91241, AA442117, AA808896, T52417, W95685, AA151139, T33151, AA610445, AA628542, AA422032, AA348728, R63854, AA574979, AA139814, AA684206, AA104614, AA210358, W98842, AA041751, AA068223, AA052848, W58896, AA145278, AA217077, AA792797, AA269756, AA183101, AA023084, AA423737, AA822385, W91432, AA145277, AA681513, AA793915, AA245973, AA790363, AA571781, AA412872, AA254535,

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#### **SEQ ID NO. 107:**

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AF040707, AF040708, AC002481, Z66370, Z83744, Z81141, AD000812, AC004609, AC002985, AC004217, AC004448, AC004128, L81694, L78810, Y09450, U63963, AL023893, AC004021, AF061032, Z68193, U36478, AC000056, X75891, Y13622, Z36000, AC004030, AC003658, Z70227, S44029, AC002558, L76523, AC002126, AC004388, S51944, AP000045. AC004216, AC004552, AF053630, AC002477, U66083, U59962, U26032, X91144, Y11740, AE001001, AA399402, AA447620, AA448454, AA069925, AA448020, AA422152, AA233630, AI039091, AA694501, AA594398, AA009713, AA156783, AA599751, AA398362, AA070017, H80269, AA938654, C02912, H80365, AA947274, AI003286, AA350419, H09156. W23160, AA298504, R40317, AA827591, AA809864, AA297589, AA809865, AA991627, AA297851, R44669, AA460451, AA082600, AA352547, AA338738, AA463393, AA555202, AA325687, R41569, R13235, H09213, AA100151, AA635653, AA302916, R19419, C03526, AA009823, AA156852, R15147, R36750, AA666086, AA340305, AA471272, AA091173, C03440, AA350420, AA421315, AA628294, AA232327, D11859, AA628519, AA699311, AA788699, R02062, H77404, AA082714, N51039, AA278486, AA348125, AA922129, AA976211, R11648, W94679, AA046821, AI005082, AA094299, T16281, T71616, W76189, W79649, AA046804, AA426618, AA452166, H09325, AA570351, T97619, H82895, AA485716, AA426080, AA541541, AA657945, AA603229, AA908744, H03358, AA424532, AA770584, AA782577, AA832194, AI037102, AA764527, W64225, AA163573, AA073941, AA619080, AA709972, W98890, W59419, AA116886, AA199485, AA754894, W70378, AA797181, AA002597, AA839076, AA387015, AA726154, AA718439, AA980485, AA270671, H35002, H35204, AA686027, AI012778, AA686254, AA684618, AA686253. AI029875, AA799580, AI045682, AI029738, AA840778, AA753356, AA697668, AA979757, AA964367.

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#### **SEQ ID NO. 109:**

M86752, AF039202, Y15068, U27830, X79770, U89984, AP000020, AL008628, U72207, D17760, U19927, U34921, U12707, M62740, J03071, AF016422.

40

## **SEQ ID NO. 111:**

U64317, L43821, AF009366, D29766, U48853, U28151, Z66513, U38481, M69181, U36909, U58513.

#### **SEQ ID NO. 113:**

D13866, D14705, L23805, U03100, X59990, D90362, Z37994.

**SEQ ID NO. 115:** 

AF011793, AJ001309, Y13350, U95727, AC002087, AC002485.

**SEQ ID NO. 117:** 

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D13627, Z37164, D42052, Z37163, M97562, Z22289.

SEQ ID NO. 119:

15

Y08915, AF000577, L31652, AJ223156.

**SEQ ID NO. 121:** 

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5

X91141, X77723, D86066, U70777, D85844, AB001750, Y08613, D38038.

**SEQ ID NO. 123:** 

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U27462, AB009517, U10399, AA972362, H16641, AA375684, AA336508, AA393076, AA211450, AA312542, AA412102, H81084, AA807300, AA517135, AA035926, AA794287, AA163888, W75621, AA521882, C94187, AA445895, AA842425, AA111773, AA051908, H35839, AA802415, D48028, AI010004, D36325, D48057, W66028, AA788342.

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**SEQ ID NO. 125:** 

U63333, AF035625, AF055320, AF032984.

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**SEQ ID NO. 127:** 

D49677, D49676, U51224, D45205, AC004106, D26474, S69507, D17407, Z74476, Z26635, Z99279, AC000056, M83200, AB009480, X86100, Y13901, X67611, X56007, U62631, X59496, Z72646, AC005092, Z98887, U19755, U41011, U63630, D10061, L20632, U57971, X94106, Z94721, U60414, M13101, X61298, X53581, U90211, X73124, U45980, U41411, AB000407, Z97355, AA601026, AA669459, N80309, AA569819, AA430135, AA723697, T67521, T67543, AA845804, AA320008, AA377829, AA028151, AA028127, AA814970, AA814962, T69519, AA331011, N78889, AA507133, AA630855, W27716, AJ003534, AA600133, AA807323, AA078585, AA326345, AA329479, AA904199, AA824460, AA424001, AA452591, AA920561, W30240, W11838, AA221247, AA050756, W20707, AA199064, AA771282, Z74661, AA545349, AA422535, AA763112, AA709977.

SEQ ID NO. 129:

D10630, U41671, X63747, Z98745, AB007886, Z11773, AL021997, X84801, U78722. AL022393, Z55026, AC004232, D88827, U31248, AC004522, U88079, U57796, AB011129, AF017433, AJ003147, U78142, AC003966, AF011573, Z21707, AF031657, U88080, U62392, U88081, X51760, X65230, X12592, M36514, L32162, U69645, L26335, X07290, L35269. X07289, L41669, M67509, D45210, D10628, L75847, L32163, U71601, U46186, X82126. X65232, X82125, Z30174, X16281, AC005261, X78933, M29580, Y00850, M88372, X77744, X52356, AF038179, M15709, M99593, X78924, U71599, U41164, X65231, U09413, L28167, U07861, D50419, X78928, X17617, M36146, U09852, X60152, X78927, M29581, AF027146, M96548, M88370, U95044, AF020591, X78925, M88360, X16282, X06021, U66561, U65897. X12593, X89264, X64413, X52533, U71600, AF025771, AF025770, U95992, U95991, U75454, L77247, X55126, AA613873, AA724783, W89121, AA873391, AA285170, W30901, AA620620, AI052471, N59279, W32455, W88914, W02805, N49069, AA011701, AA495857, AA291157, H64286, W02140, AA151132, AA424817, AA702978, F10244, AA011595, AA284023, AA370051, H64287, N77050, R08028, AA076722, R08076, AA077262, W26330, AA314608, AA226724, AA996155, AA910691, N29000, T46864, W52139, H53499, AA400924, AA453245, AA443452, F08086, AA626790, H41302, W58016, T08471, AA631964, W37662, AA776714, AI014264, AA625515, W21271, AA481221, AA115318, W44916, F06540, AA683109, AA334780, R57599, H54888, H54887, N83314, H40464, AA635153, M78146, R20489, AA402531, AA457311, R54170, F06238, H17015, AA701913, H05892, AA682749, AA974380, T77293, F06725, F06163, AA005274, H15716, AA324611. N49093, AA164237, AA535743, AA714166, W26721, AA018889, AA005168, Z21091. AA485008, AA088626, R98365, AA984447, H78732, H78719, AA130717, AA903551, AA930937, AA244891, AA161830, AI036871, AA144413, AA475739, AA756477, AA457998, AA739462, AA272875, W12178, AA140301, W62054, AA562594, AA118740, AA985880, AA017814, AA797641, W14162, AA261676, AA017765, AI036166, AA111087, W62216, W77264, AA021856, AA017906, AA155283, AA023905, W71471, AA021791, AA021779, AA023884, W14525, AA030180, W36989, AA021734, AA510240, W47789, AA240161, AA871668, AA260250, AA064077, AA036225, W75531, AA798457, AI005795, AA499468, AA799050, AA244987, AA044497, AA014148, W66907, W59409, AA615956, AA110661, AA138214, AA738624, AA184558, AA184177, AA137979, W10514, AA546639, AA536874, AA415708, AA415783, AA799270, AA726681, AA611109, AA403675, AA880983. AA611311, AA537547, AA537582, AA476109, AA064411, AI043118, AA435439, AA240059, AA289228, AA197831, AA119538, AA444998, AA153300, AA896035, AA940187, AA427224, AA920304, AA555714, AA266357, AA543703, AA416019, AA790674. AA123106, AA386765, AI047413, AA432576, AA124696, H34137, AI030812, H31100, AA494741, AI012567, AA817763, AA800215, AA800306, AA892061, AA850654, AI011599, C82417, AA800027, C83273, AA800810, AI030120, H34068. 40

SEQ ID NO. 131:

AB002374, X51966, AL021367, AF036702, U88822, AF045642, U55815, AC004518, L13696, AL021889, U75395, AC002554, AC003103, X90386, X04981, U58334.

**SEQ ID NO. 133:** 

U48587, U68267, AF001906, AF033856, M33336, U73177, J03685, AC004743, AC004539, Z60442, N53159, N75331, AI042621, AA435593, AA608757, AA076290, AA662552, AA213762, AA630025, R57980, N24985, AA813323, H21646, H05642, AA359799, AA191039, AA318867, H15234, AA323419, N27160, AA636826, AA656934, AA726211, AA619507, AA792581, W59642, AA035921, AA637995, AA667370, AA592134, AA637894, AA591158, AA756070, AA467467, AA739462, AA272875, AA214985, AA739083, AA914526, AA386742, AA919409, AI046649, W35790, AA016357, W97992, AA656026, AA414710, AI006426, AA673795, AA239695, AA285593, AA615757, AA038932, AA073580, AA103792, AA220731, C85146, AA867112, AA028705, AA118743, AI005830, AA874206, AA451006, AA667719, AA637623, AA492608, AI048487, AA189854, AA116581, AA096759, R04321, R04399, Z48427, R04620, R04065, R04404, R04422, R03209, C51162, C44210, R05229, C49234, R03208, R04273, D75630, D75447, D75141, D74833, D74636, D74299, D70237, R05254, C42102, AA658642, AA685519, AA799735, C93660, AA685980, AA750619.

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#### SEQ ID NO. 135:

AC005175, L12168, M98474, U94696, M88485, Z95972, Z81557, S54909, U59831, AB002387, U59832, AC004221, AC003993, AA505656, AI004052, AA975150, AA904315. R39951, AA908198, AA348001, AA348002, R39437, R39435, D21034, AA365146, AA813999, F12674, AA226122, T50818, AA143492, AA337395, AA003016, AA475640, W78672, AA517530, W45934, AA915424, W54264, AA168145, W11712, D34652, U92753, Z84127, U92730, AA438286, AA978864, AA941236, F14527, D47303, D15953, AA202003, AA979012, AA440964, AA736036, AA246888, AA940864.

## **SEQ ID NO. 137:**

AF064604, L63543, AE000647, AF064804, AA443401, AA334624, H69413, H69440, H69851, AA167818, AA830102, N64831, AA947764, AA453748, AA453830, R52194, T30970, AA903211, T32140, T30969, W05727, AA024651, C18655, AA386236, T69012, AA442992, AA452775, AA292522, AA223531, AA221067, AA004165, AA538370, AA067626, AA104327, AA874150, AA450950, AA692789, AA798137, AA119093, AA240418, 35 AA542585, AA520648, AA519835, AI045289, AA520246, AA849945, T75681, AA520090, AA651385, Z25578, AA585901, AA395446, C90090, AA713116, AA851675.

## SEQ ID NO. 139:

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M24603, X02596, Y00661, M15025, X06418, U07000, X52829, M19730, M30829, X52831, M30832, X14676, X52828, X52830, S72479, L02935, M64437, M17542, L19704, U01147, X07537, X14677, X14675, M17541, M17543, M19695, X76485, AF023460, X89600, U19759, AF039083, X71790, AC004679, AC002076, AF035456, M99565, Z72005, Z79997, AL021154, 45 Z98259, AC003108, L13706, AF018254, M69197, U67228, Z75887, U14661, M84472, AC005200, AC001228, AC004761, Z95124, AC002540, Z79699, AE000926, U43572, U51281, D82351, AB013379, U34879, AC002425, AC004598, AA338585, AA333142, AA126116, H55543, H55721, R54267, H55614, H55699, H55545, AA744741, AA772917. H29052, AA573543, T16608, AA773472, AA775416, AA601919, AA470534, AA351521,

AI015318, AA351163, AA486365, AA470985, AA565376, AA344993, R92629, AA553555, AA740903,

AA090392, H94289, AA457592, AI033503, T69709, R94066, AA040853, AA065296, AA349058, AA703759, T05287, H86075, AA043080, AA669995, AA737864, AA726753, AA727154, AA546638, AA222375, AA671227, AA032828, W14856, W33789, AA874531, AA982359, AA965843, AA965737, AA800560, AI035042, AA941796, AA390686, AA735566, AA802030, C74658, AA246925, AA803435, C27952, AA944566, AA817514, C83561, AA978443, C24959, C82705, C72516, H34014, AA712916, AA820781, D21893, D15866.

10 SEQ ID NO. 141:

S45630, AF007162, X95383, AF029793, M55534, X60351, S77138, S77142, S74229, X60352, M63170, M24906, M28638, J03849, M12016, M73741, U04320, M12014, M24092, L08078, S53164, U26661, M12015, M25770, U16124, X87114, D29960, X14789, X85205, M17247, U05569, U66584, M26142, U47921, U47922, V01219, X95382, AP000007, AE000869, AB009529, AF062537, D10457, S37449, X59541, AA742442, AA704135, AA211774, N35834, AA482745, AA211607, N28898.

20 SEQ ID NO. 143:

U78082, L78810, U14573, AC004068, U07561, M98511, AC004673, AA613346, AA953216, AA305926, H92800, R98218, AA629543, AA297666, AA302982, AA429481, AA126005,
AA837225, AA856961, AA946848, F13749, AA847704, AA833896, AA621381, AA833875, AA459962, H22141, N73060, AA491955, H28477, AA224463, AA708753, AA152253, AI028510, AA483606, AA992126, T54783, AA715075, AA568204, AA715173, N64587, AA570740, AA984258, AA904211, H94979, AA085410, AA599352, AA488620, AA574442, AI049845, AA593471, AA393830, AA610509, AA297145, AA113272, AA835889, AA655005, AA689351, R93919, AA613761, AA550989, AA303054, H07953, AA713815, AA827490, AA865262, AA461308, H73550, AA657835, AA362349, H82679, AA378682, AA577755, AA663472, AA490602, AA857673, AA347114, AI049630, AA086150, AI017251, AA877992, AA084609, AI050760, AA808998, AA503258, AA613138, AA603156, AA513293, R97934, AA610233, AA654874, AA501867, AA604831, N22058, AA492114, T50676, AA757426,
AA584482, AA789192, AI004591, T50694, AA862227, AA594145, AA728911, AA847499, AA159978, AA534204.

SEQ ID NO. 145:

Z69030, L42375, U37352, D26445, U38192, U38191, U37770, U38190, U37353, U59418, L76702.

## 45 SEQ ID NO. 147:

40

L07872, L34544, L34543, X17459, S63463, M81871, L08904, U60093, U60094, L07873, L07874.

SEQ ID NO. 149:

U07158, X85784, AJ000541, U76832, L20821, AC003089, AC004504, AF049236, L40609, AF053765, L14677, Z94056, Z18277, AE001073, U85969, X79283, AJ223473, AA632339, AA732931, AA610556, AA973899, AA598896, AA531553, AA826535, AI000209, AA290836, AA642711, AA085920, W22275, D20744, UMGS017, AA487868, AA487869, AA085919, 682 AA833281, AA619252, C77541, AA691960, AA763615, AA164051, AA259589, AA060475, AA254185, AA666705, AA272597, AA152985, AI011416, AA850008, H33152, AA941811.

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**SEQ ID NO. 151:** 

M13451, X03445, X03444, M13452, X66870, X76297, X14170, X99257, D14850, D13181, L12399.

15

**SEQ ID NO. 153:** 

U28918, U17714, X82021, Z98048, D17265, D17092, Z82022, L04270.

20

**SEQ ID NO. 155:** 

X54859, Z86000, AC003043, X77738, X77737, L35930, AC003084, AC000111, M89651, AP000031, U67588, X03991, AC004660, AL010261, V01515, M86251, L29376, Z71417, L78442, U00921, AC004692, AC003698, AE000742, Z49128, Z73417, Z71418, AA424638, AA442084, AA805748, AA835489, AA713576, AA502343, AA765949, AA812332, AA831755, AA417718, AA776946, AA152295, AA731660, R48791, AA150237, N51650, N52616, N52586, AA533556, AA305755, AA760877, AA729913, AA731659, AA910594, AA904521, AA372550, R48898, N50390, R08712, H83343, AA417867, AA090407, AA009846, AA927286, AA678135, AI033148, AI041408, AA235113, AA398662, M62215, W27276, AA885767, AA460155, AA742433, R19908, AA040696, AA555240, AA043160, AA292844, R53160, AA536080, N70013, N35921, N70096, AA277029, AA560610, AI046716, AA237153, W15784, AA547132, AA231089, AA170968, D46090, C61892, C64408, D34777, D35175, D35914, D37381, AA559708, D37143, C60784, AI008855, AI021808, AI009216, D68214, AA220863, D70434.

SEQ ID NO. 157:

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U43195, U58512, U61266, D89493, U36909.

SEQ ID NO. 159:

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AF069442, AF001295, M13820, M10081, AB010077, AA491075, AA446881, AA588390, AA479958, N20112, R86178, R97894, T64868, W68074, AA365195, AA928749, AI037069, AA882303, AA791693, AA822133, AI037224, AA404165, AI036575, AA499662, AA864136, AA561223, AA183703, AA647218, AA792208, W48100, D40621, AJ225487, AA294595,

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02866, H35041, AA944944, AA597316, D26977, D68334, AA685934, W88345, AA964819.

# **SEQ ID NO. 161:**

K01546, AE000468, X95549, AC004014, Z81584, L19201, X94244, X06932, U39479, X13301, AC000386, U80847, X86737, U39478, AA883211, AA610050, AA774254, AA280736, AA926725, AA459300, N55370, AA233666, H90342, T66839, H91250, AA856968, R92873, AI034196, AI014787, AA910410, AA088535, AA230765, AA467238, AA397279, AA420226, AA396042, AA200070, AA165873, AA762534, AA067133, AA065429, AA185092, AA572057, AA111387, AA175824, AA881071, AA571692, AA104279, AA733670, AI008804, D86670, C67200, D41938, AA141467, D35894, AI001643, AA957220, T37355, T18792, D47809, W21723, AA898504, AA951903, AA661025, AA949796, AA990685, AA661449, AA948837, R04787, D16046, AA439636, AA246769, AA978829, D43523, T02021, AA803212, D22651, AA201227, AA694728, AA891643, D23309, AA820831, D41871, W21774, D16065.

## SEQ ID NO. 163:

20 X15183, AF028832, D87666, J04633, L33676, X07270, U94395, M27024, M30627, X16857, X07265, M36830, M30626, AA669137, AA725103, AA890496, AA314095, AA554815, AA313331, AA730100, AA214035, AA876412, AA121630, AA314010, AA927532. AA968674, AA679253, N66271, AA558907, AA309988, AA587079, AA075436, AA160964, AA205657, AA214083, AA130903, AA917032, AA149623, AA857523, AA889843, AA305037, AA491055, W73240, AA255644, W73295, AA765431, AA178947, N66409, AA074895, AA306976, AA075052, AA075387, AA130892, AA857443, AA405942, AA629891, AA152004, AA129550, W56527, AA513807, AA703828, AA223171, C75280. AA889155, AA854676, AA773063, AA774999, AA152392, AA307057, AA316954, AA657352, AA522607, AA188113, AA026444, AI003623, AA312717, AA312400, T64299, AA178992, AA228992, AI042136, AA457613, AI032857, AA164461, AA625127, AA807763. AA130815, AA054695, AA937097, W93534, N67875, AA526896, W52802, AA527942, N34251, W28646, AA668543, AA496091, W52511, AA070581, AA306826, AA120908, AA699607, AA086423, N72134, AA630369, AA564649, AA046806, AA666249, AA306893. AA225404, AA127417, AA854951.

## **SEQ ID NO. 165:**

M23885, AF047868, AF017732, AB005249, Z83229, AF026483, U97194, Z67884, Z67881, X13481, X07651, AC001226, AC002542, AB002307, AA984684, AA017533, AA306600, AA261957, F08123, R17885, AA282208, H85861, H85836, AA593150, H87276, AA057384, AA243602, AA013399, AA374926, AA721341, R88896, AA021538, AA101740, AA375314, AA090398, H86058, AA984556, AA215816, AA092672, AA034243, AA328017, F11174,
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AA239037, AA672620, AA915168, AA863498, AA123378.

SEQ ID NO. 167:

Y11251, AF030234, AF043945, L40407.

SEQ ID NO. 169:

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U33822, X61838, AA572230, AA589570, AA929790, AA104830, C81582, AA271190, AA290278, AA543616, AI043207, AA107832, AA958460, AI020992, AA795905, AA277468, AA475069, AA111610, AA389139, AA154163.

15

**SEQ ID NO. 170:** 

D32050, D16969, AC004423, S81497.

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**SEQ ID NO. 172:** 

D86982, L07131, M14544, AA296228, AA318436, AA296234, H88394, W26642, AF038251, AA394101, N35855, N56791, N35444, AA147382, AA647547, AA939939, AA895989, AA122437, AA277698, W75741, AI036117, AA980469, AA033178, AI006694, AA980625, AA033190, AA175922, AA172918, AA895209, AA028700, AA416048, AA175247, AA217057, AI045760, R64866, D40836, D41873, AA509279, D40089, AA114361, AA751642, AA848690, AA800525, AA802510, C24001, AA841755, AA882663, D40069, AA433358, D40199, AA958134, AA072494, AI008727, AA618978, AA848687, C21884, AA113662, AA945653, AA660093, C58446, AA908068, AA532100, AA264560, AA426658, AA097169, AA751535.

SEQ ID NO. 174:

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Z81364, AC003033, AE000665, AA570483, AA532739, AA526905, AA725306, AA134415, AA651838, AA481316, AA600310, C04532, AA004615, H20713, AA913640.

40 \_SEQ ID NO: 176

M14695, X02469, X60012, M14694, X01405, K03199, X60015, X60016, X60011, X60018, X60019, X60014, X60013, X60020, AF021816, X16384, L20442, U48957, U48956, X60010, S83123, X90592, U74486, D49825, X81704, X81705, U43902, AJ001022, D26608, D16460, L37107, AF060514, S77819, X13058, D86070, U50395, U07182, U90328, Y08900, M75144, Y08901, U74487, U48619, K01700, M13872, AF051368, U48616, U48618, X00741, M13874, M13873, X01237, U48617, M22887, X54156, U94788, M13115, U41451, U41452, X01236, K02110, U59757, M22895, M13118, U63714, M22888, M13116, M22894, M13117, U51857, U37120, U62133, U07020, X91793, L07907, U26741, U59758, S78456, L23634, U22145,

X00879, X00881, S77930, S78457, U66066, D63399, U44835, L07908, S57234, D63405, L27630, M22896, U07019, D63404, M13119, X13057, D63402, M75145, D63401, L12046, AA373960, H61357, AA358870, AA928725, H90357, AA302363, R94782, W24142, AA448185, AA004394, AA376121, AA151197, W76037, R82621, AA157426, AA343323, AA301677, AA002978, AA966981, AA839925, AA982800, AA030090, D77246, AA184043, AA142337, AA529242, AA874521, AA048636, AA168688, AA032325, AA881664, AA529082, AA874036, W06121, AA520602, R86591, AA848372, D37535, AA433405, C72790, AI009692, C25990, X91325, D71516.

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# **SEQ ID NO: 177**

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#### **SEQ ID NO: 178**

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Z50194, U92983, U44088, AC003101, X72892, AF035444, M32474, AF019953, AC001228, Y15443, AF001294, U12418, X06956, M31176, AF015277, AF002708, R43556, AA088367, AA313553, H92530, AA376262, T09403, AA814143, R75643, AA479005, AA773048, AA507143, AA402127, AA430292, AI015600, AA393069, AA463606, AA885498, AA460759,

AA398766, R48359, AA426107, AA909990, AI017459, AA076224, N39533, AI026941, AA412699, AA292828, AI024759, AI016910, AA573306, R48386, AA065307, AA774549, AI016070, AA884918, AA431512, AA306051, AA476440, AA292924, AA621059, AA411830, AA405079, AA596171, AA989987, AA472637, AA690249, AA691927, AA792720, AA637983, AA020137, AA097337, AA117759, W17615, AA285526, AA111347, AA208823, AA879750, AA413058, W33316, AA161891, W41259, AA511152, AA027481, AA020252, AA033106, AA965045, D41048, AI031042, D48020, AA925258, D40853, AA945674, C19585, AI013412, T15040, AA541011, AA990782, AA851306, AA540938, T23386, AA783863, AA979035, AA951002, AA438957, AA979006, AA978995, AA800046, AA556128, C27411, D15562, T20348, AA966363, AA949269, AA785774, AA728671, D16092, N37869, D48782.

# **SEQ ID NO: 179**

Z50194, U44088, U92983, U12200, AC004147, X82200, Z81527, M63469, Z35494,
AC003018, AL021408, M92281, AA576961, AA088194, AA258396, D79238, N27861,
AA857168, N35619, N40634, N73008, N21585, AA332511, D56582, D12298, AA641278,
Z21892, H92531, AA113084, N76094, N31261, AA227469, AI038845, AA520982, R16910,
AA380178, AA238335, AA255056, AA981576, W35008, AA238181, AA739268, AA061742,
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# SEQ ID NO: 180

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# **SEQ ID NO: 181**

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U52191, D87072, AL022162, AL008710, Z83850, AF055066, AC004254, L25270, AC003013, U53141, AL021728, AC004997, M38703, AC004020, U91321, AP000041, Z69921, AC002551, D87016, X54171, AF055481, X83213, L05489, AC003018, AB009056, AC000069, L81890, AD000685, AC003031, AC003030, Z99715, AF043301, AE000664, AF007544, X15547,

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#### **SEQ ID NO: 182**

U93574, Z84720, U93573, AC004389, AC003080, Z79699, Z83313, M22334, AC002379, Z81145, AC002523, AC004554, AC003015, U93572, AC000057, U09116, AC004769, AC005195, AL009173, Z82195, U93564, U93571, AC004216, U91324, AC004615, AC004513, Z68344, AC002556, Z97181, AC003085, AC003106, Z83827, AL009177, AC004048, L11910, U93563, U93566, AC002541, U93569, U63313, AF011889, AC002385, Z93403, AC002416, AL021069, AF051934, Z81001, Z81008, U93562, U93570, AC002076, AJ229042, AC004081, L19092, L19088, M22333, M80343, AC004673, M80340, AC000111, AC005248, AC004029, AC004103, AC004519, AC002461, U93567, U93565, AF003535, Z98754, U93568, AC003689, AC002106, AC003678, AL020991, Z92844, AC002083, AL008987, AC004142, AC004592, AF064865, AC004014, AL030998, AF036235, AC003090, AC002468, AC004381, AC002426. AF064862, Z75741, AP000034, AC002980, AE000659, AC004694, AC003667, AC002381, Z73639, Z70042, AC004677, AD000091, Z68289, AA484141, AA164621, AA604538, AA481622, AA496279, AA984452, AA767964, AA984451, AA736469, AA515158, AA179891, N23655, AA613334, AA804967, AA167491, AA502863, AA736468, AA865990, AA557741, AA577777, AA434354, AA077547, R87956, AA130610, AA458671, AA515147, AA249258, AA577804, AA370897, T51061, AA558463, AA564249, AA654792, AA937758. R14500, AA218754, AA808887, AA552844, AA610148, AA360863, AA131481, R14820, AA679387, AA604228, AA219167, AA528769, AA167264, AA211914, N44646, AA583372, AA332799, AA434071, AA768268, R67785, R11143, AA160931, AA492047, AA483907, AA018362, AA565136, AA148747, AA446799, T68944, AA622590, AA148366, AA321287,

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## **SEQ ID NO: 183**

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**SEQ ID NO: 193** 

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# 15 SEQ ID NO: 194

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# **SEQ ID NO: 195**

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# SEQ ID NO: 197 U47742, AB002381, AJ000729, L42550, M33956, AC002991, X01380, X05424, K01964, AB003499, M32660, AA248767, AA219722, AA504689, R41711, AA296844, AA492416, R51283, AA049428, AA217923, AA607511, AA689975, AA015159, AA163336, AA791924, W84145, W85185, AA097378, W18536, N28107, AA592602, AA543587, AA030663, AA881846, C81003, C80991, W08678, W66831, AA184127, W29542, AI013408, AA201942, C23941, T38919, AA042496, AA699041, AA699045, AA924655.

## 45 SEQ ID NO: 198

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# **SEQ ID NO: 199**

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# SEQ ID NO: 200

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# 35 SEQ ID NO: 227

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#### 15 SEQ ID NO: 231

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# SEQ ID NO: 235

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### 5 SEQ ID NO: 241

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### **SEQ ID NO: 244**

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AC004381, U29082, AC002078, U39655, M33582, M94080, U53344, AC002451, X16549, D10040, X16553, Y12025, U50193, AA837145, AA412384, AA602982, AA478697, AA115419, AA587840, R76363, H81547, H67227, H83962, AA665443, AA133086, AA251488, AA976922, AA662495, AA301274, AA132987, AA169423, N62994, AA722928, AA478563, AA013476, AA579347, AA501519, R76688, AA629042, AA018206, AA252018, N79902, H70300, AA644296, N23634, AA127071, F02250, AA716541, R41716, AA125908, AA662818, N79270, N62138, N64551, AA236462, AA436025, AA962585, R43118, AA115152, R49041, F02743, AA125794, AA281970, AA639166, AA127093, AA573768, N94499, AA877109, AA449432, AA608686, Z40901, W52069, AA688218, AA398554, F02957, AA347035, W73300, AA061413, W96984, AA530599, F14212, C22934, AA926098, C92915, D27726, AA924800, AA923860, C55124, AA892301, AA549967, AA751821, AA945020, D32818, AA901415, D64416, C52515, C35274, AA751972, AA568080.

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#### **SEQ ID NO: 261**

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- 45 N62994, AA013476, AA018206, AA644296, N23634, R49041, F02743, R43118, R41716, W73300, AA334995, N90126, AA061413, AA530599, W96984, AA163443, AA612360, AA919946, AA967393, C81197, AA163825, W33363, AA940335, AA522025, AA238429, AA915211, AA518646, AA930778, AA275870, AA177383, AA119983, AA058115, W12739, AA168575, F14212, C22934, C55124, C52515, C92915, C35274, C51698, AA549967, D32818,

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AI003321, T03830, AA192826, R19610, W28150, AA324720.

#### 35 SEQ ID NO:265

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#### 15 SEO ID NO: 270

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30 SEQ ID NO: 271

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X82202, X02796, T80545, AA350567, R18632, W95135, AA232983, AI022235, AA233369, AA778816, AA856332, AA107526, AA163393, AA560074, AA871746, AA016332, AA015494, W66852, AA163094, AA919948, AA733777, C26223.

**SEQ ID NO: 273** 

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**SEQ ID NO: 274** 

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**SEQ ID NO: 275** 

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#### **SEQ ID NO: 278**

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# 30 SEQ ID NO: 280

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#### 15 SEQ ID NO: 283

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#### **SEQ ID NO: 285**

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### **SEQ ID NO: 286**

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#### **SEQ ID NO: 287**

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### 40 SEQ ID NO: 288

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### 25 SEQ ID NO: 289

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AA815140, Z45678, AA393239, H70916, R42609, W74150, W46431, W74157, AA811026,
H12391, C16126, AA291279, H70913, AA553046, AA277240, AA390010, AA289068,
AA066355, AA259657, AA880335, AA063857, AA203797, C77689, AI050209, AI026596,
C52662, D33733, C93027, C57696, H33415, AA696819, C70316, AA858626, AA859618,
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N37856.

### 35 SEQ ID NO: 316

U56860, U00035, Z69251, AC003686, AC004774, AC002457, AC001527, L81869, Z82253, AL022101, AC002485, U39648, AC003085, Z74043, AL022104, X85105, Z70177, AC004227, AF002197, AC004478, Z71263, AC000378, Z82212, X67744, AA809784, AA412105, AA836191, AA827109, AA804427, AA814890, AA768944, AA354395, AA829438, AA828744, AA205333, AA782931, AA250965, AA251165, AA151555, AA256169, AA789094, T79588, AA426431, H79702, AA029448, R21432, X71647, AA512108, AA189682, AA739022, R04648, AA417407, AA851163, R03957, R05178, R03268, R03852, C25737, D33134, R03421, R03256, C34891, D37751, D72823, AA956678, AI007798, T39037, AA294340, AA898159, C61838, D69030, AA850706, D65552, C62086, AA851036, C52237, AA925983, C32833, AA294788, AI030007, AA998684, AI011286, AA800269, AI009727,

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#### **SEQ ID NO: 317**

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#### **SEQ ID NO: 318**

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#### 25 SEQ ID NO: 319

AC005191, AC000022, AC004161, U67949, D32002, U48251, X80030, T34938, AA348735, T11294, AA496625, H11830, F11832, AA037681, T65508, AA011609, H71333, H15581, AA496503, C15755, D81192, D81591, AA234424, T83538, AA461155, AA025279, Z36730, D80564, AA234423, N26354, W00688, AA692746, U37159, C39409, C91297, AA799289, D68368, AI029040, AI007668, C08934, AI010541, AA850556, AA392473, H31325, D34571, AI043892, AA996460, AA946179.

## 35 SEQ ID NO: 320

AC004142, Z70750, AC004766, Z78416, Y13473, U80452, AF000299, U88173, AA702479, AA702790, AA825557, AI038962, AA505372, AI051720, AA505567, AA864908, AA505703, AA610492, AA505302, AI015179, AA704244, AA037682, AA664420, AA505301, AA147170, AA814618, AA321331, Z40775, T35671, H15525, AA011610, AA633691, H11751, AI025182, H11079, T65428, AA705344, F09480, AA811013, AA091593, AA938978, AA089924, AA722822, W32680, AI050875, H01026, W67301, AA890360, AA678583, R49664, AA815086, C16979, AA507270, AA558990, N70810, W80778, AA883720, AA790780, AA275189, AA600642, AA265030, AA259672, AA855284, AA866847, AA792675, W57074, AA990198, AA607249, W75269, AA789988, AA259316, AA790623, AI021000, W57110, AA990198, AA067249, AA726260, AA537135, AA798563, AA755019, AA030169,

AA116306, C23464, AI012480, C23465, AA201498, AA802376, C91292, AA246870, C90701, AA963602, AA950424, AA956932.

# 5 SEQ ID NO: 321

AE000658, U85195, AB009521, Z70288, M12922, T52127, AA325912, T95858, T64635, T07307, H80456, T95864, T50392, AA833739, AA977526, AA948672, T53866, AA029491, F10380, AA132333, AA455988, R41594, R43657, AA132348, R44944, AA909207, AA694319, D31584, AA672225, AI019267, AA738911, AA467723, AA066186, C19110, Z37608, AA186306, AA392283, AA605525, C70333.

# **SEQ ID NO: 322**

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Z83836, M59371, Z69917, AC004768, Z75895, Z39710, H09245, R39824, F03749, AA493590, AA747004, AA411065, H83531, AA315999, AA437325, Z28508, AA583390, AA426377, AA252549, N76310, H78530, AA768319, AA822118, W66967, W62965, AA616290, AA839391, D19329, AA036227, AA185213, AA072651, AA072847, AA024238, AA244792, AA671995, AA415475, AA438233, W64263, AA097649, AA245717, AA000795, AA475421, AA072855, W99134, W61778, AA184000, W33766, AA185206, C78177, AA798172, AA863961, W81788, W53793, W62573, AA230836, AA466643, C78205, AA822043, AA086975, AA990223, AA655533, AI049173, AA790279, W97047, AA980600, W29472, AA752374, D41474, AA899904, C26152, T14820, AA818727, T14914, AA893758, T22262, AA817000, N65632, AA816371, Z29789, AA394995, AA816959, T46743, AA941188, AA950659, AA849737.

## SEQ ID NO: 323

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Y13472, AF012126, AF060181, AF035374, D63790, S53307, S53301, AL021713, Z98949, AF039713, M30114, D89168, U02512, M57504, AF060205, M69019, AF033029, D00863, U55369, M13655, AL021816, M57505, M11969, AL024485, Z82189, L13855, X03636, U02513, AA329832, T48184, AI028699, AA884702, AA091936, W38657, AA863120, R72495, AA486001, H91730, AA681096, AA793734, AA981374, AA675674, AA690226, AA981061, AA880265, AA437687, AA472881, AA437673, AA591866, AA792627, AA088934, AA073408, AA795731, C42637, C62662, L47042, AA787536, D22851, D15739, AA532235, AI026532, T43691, H98444, R29968, C27630.

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## **SEQ ID NO: 324**

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## **SEQ ID NO: 325**

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## **SEQ ID NO: 326**

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### 35 SEQ ID NO: 327

AF060181, Y13472, AF012126, AF035374, S53307, D63790, S53301, Z98949, U15304, M57504, M69019, U02513, M30114, AF033029, U02512, M13655, AL024485, Y10259, D89168, L13855, M11969, M57505, AL021816, X03636, AA329832, T48184, AA486001, AA091936, R72495, AA863120, AA793734, AA675674, AA681096, AA690226, AA981374, AA710968, AA880265, AA437673, AA437687, AA472881, AA088934, AA073408, C92164, L47042.

## 45 SEQ ID NO: 328

Y13472, AF012126, AF060181, L28807, Z49809, AF043695, X07891, AC001052, Z98601, M22874, AC004445, AC005198, AC004114, U35852, Z48444, AC001648, Y07564, AC003945, M22876, X05643, D31712, Z69666, AF009615, M22875, AC004356, M38643, AA282776, AA993582, AI051311, AA767826, AA860937, AA251581, D11944, AA629081, AA872477, C14749, AA872945, AA663837, AA863063, AA034499, AA452155, AA505638, N79268, AA251580, AA283078, C14507, C14328, C14354, AA115537, AA135989, N71855, D80504, D81220, AA746706, AA370561, AA370562, AA452383, N57805, N62550, AA843321, W37572, H97032, N30488, N38781, R93033, AA514700, AA091256, AA635156, AA704735, H69847, AI038776, T07543, T41024, N77224, AA267676, AA798296, AI047555, AA161918, AA960263, AA254301, AA210440, AA497405, AA497406, AA117254, AA051239, AA137972, AA821741, AA926013, AA851515, AA950193, AA695692, C93891, AA394737, AA957795, C61851, AA799762, AA943258, AA417542, AA644744, AA957887, AA848449, AA818311, AA997643, AA956886, AA882675, C64092, AI007952, AA851240.

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**SEQ ID NO: 329** 

M90309, M96256, M90820, D82876, M95123, U62545, AE000387, U83435, AC003982, U28379, Z81081, AC004309, M29192, U64849, U23170, U58751, Z79999, AA662136, AA626635, AA507452, AA805078, AI039677, AA745880, AA722415, AA133371, D56262, AA514235, AA425201, AA946647, AA830458, AA083192, AA207200, AA316768, AA180767, N63329, AA878427, AA934449, AA133184, AA402087, AA937256, D52197, AA687770, AA365011, AA083191, AA731077, AA196815, AA211880, AA305565, AA099456

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SEQ ID NO: 330

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AA044047, AA092160, AA346981, N85021, AA248133, AA368106, W22634, AA694482,
AA770656, H86231, T78778, W03714, AA258169, AA565536, H56510, AA769400,
AI035782, AA030804, AA033212, AA049640, AA734288, AA838966, AA734000, AA929708,
AA939398, W71206, W39990, W39917, AI006564, W35012, AA985693, AA967387, W71004,
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AA037985, AA259405, AA423660, AA289830, W70655, W65892, AA763976, AA563018,
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AA752205, L38123, D35571, D39195

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**SEQ ID NO: 333** 

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AA545793, AA853932, AA853320, N86419, AA852349, Z17837, R57888, AA429966,

AA368106, AA694482, AA770656, H56510, H86231, AA769400, AA258169

AI035782, AA030804, AA033212, AA049640, AA734288, AA838966, AA734000, W71206, AA929708, AI006564, AA939398, AA985693, AA967387, W71004, AA143948, AA162315, AA562776, AA563168, AA874667, AA117341, AA855746, C82438, C83294, AA495069, D39195, L38123, D35571, KM252/T3,

#### SEQ ID NO.334

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D89937, U06863, M91380, U06864, AE000337, D90880, X64696, AC002326, AL008732, AL009031, M32756, U23172, D89937, AA545793, Z17837, AA853320, AA852349, N86419, R57888, AA429966, AA044047, AA092160, AA346981, AA853932, N85021, AA248133, AA368106, W22634, AA694482, AA770656, H86231, T78778, W03714, AA565536, H56510, AA545793

#### SEQ ID NO.335

Z68106, AC004770, Z75714, Z85994, AL021939, Z71260, U36840, Z82090, AJ224445, AE000348, D83479, U21323, Z68106, AA716497, H98974, AA703998, AA044900, AA044689, AA031932, AA491463, AA599783, AA032050, AA186359, AA173933, AA600033, H97601, W63570, AA627069, W72045, AA025046, AA548128, AA088246, W58303, AA669937, W52070, H97416, AI041635, W52215, H97549, AA137262, W46845, W92629, AA128494, AA026782, W76397, AA661793, W94840, N79437, W46494, AA595373, W78218, N23437, W94418, W46918, N34381, W46790, AA583657, AA599353, AA961557, W58194, N33105, W42793, W96120, H50538, W52141, W81572, AA593009, AA983246, H97340, AA147651, R95788, N67716, N58122, T47507, AI025353, AA888923, W96121, AA722567, AA788950, W74255, AA188212, R56693, AA987381, AA565505,
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#### SEQ ID NO.336

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### SEQ ID NO.337

45 AF012072, U04282, U93694, AJ229042, AF051934, AL010167, AL008970, AF005680, X56564, Z81472, Z48717, AF005697, AF014948, AC004414, AF005683, AF005681, U04280,

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#### SEQ ID NO.338

M90820, M90309, M96256, M95123, D82876, U62545, AC003982, U64849, U23170, U97592, AC004099, U58751, M29192, M90820, D56262, AA662136, AA316768, AA180767, D52197, AA196815, AA083191, AA305565, AA099456, AA211880, AA425201, AA374550, D54751, AA904934, AA301380, H16000, AA304018, AA330777, AA661783, C03243, AA083192,
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AA219658, AA430392, AA631802, AI040805, T09413, T33924, H05237, AA768012, D56262.

# 30 SEQ ID NO.339

M90309, M96256, M90820, D82876, M95123, U62545, AE000387, U83435, Z81081, U28379, AC004309, Z79999, M90309, AA662136, AA626635, AA507452, AA805078, AI039677, AA745880, AA722415, AA133371, AA514235, AA425201, AA946647, AA830458, AA083192, AA207200, N63329, AA878427, AA934449, AA133184, AA402087, AA937256, AA687770, AA365011, AA731077, AA515865, AA910956, AA180767, W67861, AA301380, D56262, AA182893, AA330777, AA358517, AA661783, W67804, AA652387, AA316768, AA523222, AA541535, AA305565, D57347, AA662099, AA904934, H16000, AA211880, AA083191, AA196815, D52197, AA099456, AA091762, AA886161, AA876833, AA928813, AA512845, AA374550, D54751, AA304018, AA809606, AA836660, T23842, C03243, AA709130, AI023221, AA287349, N29511, AI015577, H80862, AA701928, AA815104, W46860, AA856607, AA929000, W89194, AA446792, T61548, AA913564, AA828597, AA662136.

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X59417, X61972, D10755, AF056191, Z72533, S58126, M55440, M63641, M22647, AC003026, L11235, D82813, Z68870, D82812, X59417, AA029397, AA837580, W23501, AA890064, AA488257, AA632149, AA703270, AA890484, W53005, AA716489, AA446816, W44361, AA316602, AA843688, W20013, W52807, W44618, AA526876, W39027, W49827, W60039, AA315539, W38864, W40517, AA583625, W17240, W67897, W03417, AA126319, AA772085, W32916, AA315426, W19376, W46657, AA860293, W31060, W94046, W37276, AI024374, W77914, AA523299, W24607, AA044357, W40204, AA505371, AI034269, AA448491, AA844258, AI041663, N50564, AA807830, R52324, W47241, N29205, W00352, H21413, AI014835, AA716549, AA861938, AA612828, T29583, AA045467, AA329485, AA661664, W94047, AA372064, T89588, AA044173, AA863108, AA488200, N93220, AA570625, AA612774, AA716138, T95448, AI052107, AA916452, AA861538, AI032881, AA722960, AA652222, AA946746, W53006, AA860602, N50621, H06545, AA973433, AA164391, AA301799, AI026047, AA843370, AA706945, AA229044, N50137, W44599, W05095, AA724169, AA989387, AA353184, AA916455, AA029397.

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# SEQ ID NO.341

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# 30 SEQ ID NO.414

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- 45 SEQ ID NO.420

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AF055066, D87742, U03517, AE000786, Z77661, U96410, AC002534, AC003671, AF045635, AL023828, Y13027, X14564, AC002133, L25599, AF016485, AF038667, AB005248, Z99280, U00066, N22700, N26671, N39824, N31174, AA852538, AA309729, F05933, AA300297, N52860, AA429602, AA432213, AA004740, AA600042, AA333530, R39564, R37509, H10751, AA779571, R21849, R22978, AA326278, AA828131, AA779268, AA021539, AA134969, R33584, AA272205, AA198541, AI050266, AA008780, W50581, W54065, AA013712, AA790199, AA530506, W39795, W47859, AA544020, AA285935, W78367, AA541855, AA756426, AA543223, AA407351, AA049905, AA980096, AA198960, W59406, AA543470, AA051746, AA051740, W63897, AA543462, AA549928, H35214, C22086, AA540625, C44615, C44702, C66923, AA536593, C50811, C45621, AA695657, C43409, C42954, C39471, AA566406, AA802971, C22260, C09924, C08764, D75395, D74740, R30020, AA997324, C42563, AA996401, AA695316, AI011725, AA956731, C69349, D70026, C09085, AA697043, C47594, C44847, AA956205, AA951676, AA824226, C49923, C47102, C90229, AA685785, C68943, C49315, C45448, C09296, L47915.

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- 30 AA867100, U91685, AA166356, AA153041, AA200270, AA981316, AA891230, AA848299, AA924412, AI008010, C91817.

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- 40 AI002203, H09138, AA297027, AA417202, AA991752, AA976655, AA621848, AA481261, W45634, AA811477, AA694317, AA330583, R68013, AA058932, AA286960, N45566, AA287919, AA731027, T71098, H92640, N40079, N44797, AA707671, AA464675, AA253389, H45906, AA968917, R64206, AA431091, AA773762, AA253414, AA731754, H42129, N32469, N90240, AA743738, T58992, AA455204, AA794141, AA245190,
- 45 AA110302, AA178023, AA673874, AA212119, AA274662, AA895062, , AA901423, AI029474, AA875475, AI012039, AA799473, AA942674, AA924688, AI010780, AA787461,

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## SEQ ID NO.416

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# **SEO ID NO: 439**

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## **SEQ ID NO: 455**

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# 25 SEQ ID NO: 457

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**SEQ ID NO: 466** 

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**SEQ ID NO: 468** 

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# **SEQ ID NO: 470**

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# 35 SEQ ID NO: 471

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AA780367, AA625308, AA541794, AA577881, AA364984, AI041182, R94501, AA283813,

45 AA868298, R48891, AA878456, AA908775, N20359, AA083294, D79816, AA614109, AA834129, AA490741, AA873006, AA635369, AA283812, AA810086, AA991313,

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5 SEQ ID NO: 472

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# 15 SEQ ID NO: 473

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#### **SEQ ID NO: 474**

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#### **SEQ ID NO: 476**

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#### 25 SEQ ID NO: 479

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# **SEQ ID NO: 480**

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X83973, AC004585, M92280, U32712, U61958, L25598, D63880, M31229, AC004002, X67320, U46596, X60325, U73644, AC002396, X89870, U72499, R62169, AA206573, H04110, AA135261, AA025528, AA218774, U69197, T31173, H17179, T31172, W28253, T74327, R95466, T06248, AA191685, AA209495, AA285302, T11250, T10730, AA877091, T30286, AA813637, AA700898, AA918411, AA890493, U25927, AA156216, AA240112, AA270608, AA896810, AA153656, AA106767, AA003959, AA562089, AA104976, W82776, AA008221, AI007191, AA797994, AA396048, AA003400, AI034962, AA597427.

**SEQ ID NO: 482** 

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# **SEQ ID NO: 483**

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# **SEQ ID NO: 484**

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# **SEQ ID NO: 485**

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# 30 SEQ ID NO: 487

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# 10 SEQ ID NO: 490

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# 25 SEQ ID NO: 491

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# 25 SEQ ID NO: 498

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#### 40 SEQ ID NO: 499

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**SEQ ID NO: 501** 

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**SEQ ID NO: 502** 

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**SEQ ID NO: 503** 

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**SEQ ID NO: 504** 

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**SEQ ID NO: 506** 

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### 20 SEQ ID NO: 507

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# 35 SEQ ID NO: 508

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**SEQ ID NO: 509** 

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**SEQ ID NO: 510** 

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SEQ ID NO: 511

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**SEQ ID NO: 512** 

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- 40 AA076343, AA296715, AA076342, AA353626, AA015595, AA081221, R83719, AA334546, H51631, AA343126, T85486, W22495, AA129429, T20065, R96799, AA443644, T78812, AA864764, N53004, W48656, AA599769.

# 45 SEQ ID NO: 514

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#### **SEQ ID NO: 516**

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# **SEQ ID NO: 518**

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5 SEQ ID NO: 519

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**SEQ ID NO: 523** 

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SEQ ID NO: 524

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**SEQ ID NO: 525** 

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**SEQ ID NO: 527** 

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**SEQ ID NO: 531** 

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20 SEQ ID NO: 532

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**SEQ ID NO: 533** 

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SEQ ID NO: 534

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**SEQ ID NO: 535** 

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**SEQ ID NO: 537** 

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**SEQ ID NO: 538** 

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# 40 SEQ ID NO: 539

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SEQ ID NO: 541

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**SEQ ID NO: 542** 

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AA927565, AA805306, AA774869, AA379994, R14378, AA305260, AA214396, H47665, AA043190, F13037, T08367, N28912, AA627345, AA702321, AA344594, AA721753, AA446322, AA415277, AA171097, AA444428, AA982781, AA000614, AA717988, AA940013, W53574, AA718011, AA221937, AA833125, W10683, W09810, AA914615, W64914, D77216, AA738699, AA197530, AA762162, AA119104, AA096888, AA955830, H33467, AA052021, AA007704, AI044010.

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- AA971158, R71133, AA948444, AA379373, AA770375, AA836690, AA811802, AA806363, AA496170, AA080102, AA104575, AA110087, AA111451, AA104058, AA098398, AA104601, AA389459, AA087347, AA407529, AA655129, AA870247, AA098304, AA415317, AA111471, AA110512, AA104790, AA542353, AA107448, AA500811, AA517402, AA072168, W36221, AA619786, AA682146, AA200846, AA038054, AA562718, AA637070, AA817421, AA736032, L46413, C12590, C73485, AA924572.

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- 45 AA052401, D18981, AA522251, C87048, AA986473, AA002573, AA924151, AA943376, AA899268, D35942.

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30 SEQ ID NO.3

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# 40 SEQ ID NO:597

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# 25 SEQ ID NO:599

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WO 99/04265 PCT/US98/14679

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# SEQ ID NO:600

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# SEQ ID NO:601

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# 5 SEQ ID NO:603

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# SEQ ID NO:604

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#### SEQ ID NO:605

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# 30 SEQ ID NO: 650

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#### 40 SEQ ID NO:658

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5 SEQ ID NO:659

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#### 30 SEQ ID NO:660

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45 SEO ID NO:662

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### 5 SEQ ID NO:666

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WO 99/04265 PCT/US98/14679

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# 20 SEQ ID NO:673

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AA042872, AA042872 zk56b07.s1 Soares pregnant uterus NbHPU Ho... 543 e-152 T08932, T08932 EST06824 Homo sapiens cDNA clone HIBBM46 5' end. 537 e-150 AA488258, AA488258 ad08f07.rl Soares NbHFB Homo sapiens cDNA ... 533 e-149 T19350, T19350 h03012t Testis 1 Homo sapiens cDNA clone h0301... 496 e-138 H87681, H87681 yw15e04.rl Homo sapiens cDNA clone 252318 5'. 490 e-136 H81522, H81522 yu61h08.rl Homo sapiens cDNA clone 230655 5'. 466 e-129 T49620, T49620 ya77g03.s1 Homo sapiens cDNA clone 67732 3'. 452 e-125 R14363, R14363 yf80d10.r1 Homo sapiens cDNA clone 28995 5' si... 446 e-123 AA211476, AA211476 zp75h11.s1 Stratagene HeLa cell s3 937216 ... 430 e-118 N46636, N46636 yy48a09.r1 Homo sapiens cDNA clone 276760 5'. 424 e-116 Z17358, HSDHII065 H. sapiens partial cDNA sequence; clone HI... 416 e-114 R40737, R40737 yf80d10.s1 Homo sapiens cDNA clone 28995 3'. 400 e-109 AA410278, AA410278 zv32f05.r1 Soares ovary tumor NbHOT Homo s... 383 e-104 AA496574, AA496574 zv37b03.s1 Soares ovary tumor NbHOT Homo s... 375 e-101 N34907, N34907 yy48a09.s1 Homo sapiens cDNA clone 276760 3'. 371 e-100 T49619, T49619 ya77g03.rl Homo sapiens cDNA clone 67732 5'. 355 1e-95 AA301480, AA301480 EST14551 Thymus III Homo sapiens cDNA 5' end 341 2e-91 R31593, R31593 yh76f03.s1 Homo sapiens cDNA clone 135677 3'. 317 2e-84 AA984591, AA984591 am89d10.s1 Stratagene schizo brain S11 Hom... 313 4e-83 AA338831, AA338831 EST43831 Fetal brain I Homo sapiens cDNA 5... 238 2e-60 T07305, T07305 EST05194 Homo sapiens cDNA clone HFBEG86. 230 4e-58 AA159942, AA159942 zo79c05.rl Stratagene pancreas (#937208) H... 204 3e-50 R57355, R57355 F2878 Fetal heart Homo sapiens cDNA clone F287... 196 6e-48 AA729237, AA729237 nx35c08.s1 NCI\_CGAP\_GC4 Homo sapiens cDNA ... 192 1e-46 AA877709, AA877709 nr09g11.sl NCI\_CGAP\_Co10 Homo sapiens cDNA... 172 9e-41 AA969195, AA969195 op51c03.s1 Soares\_NFL\_T\_GBC\_S1 Homo sapien... 107 4e-21 AA327432, AA327432 EST30768 Colon I Homo sapiens cDNA 5' end 80 le-12 AA854147, AA854147 aj71f01.s1 Soares parathyroid tumor NbHPA ... 74 6e-11 AA983156, AA983156 oq51g09.s1 NCI\_CGAP\_Kid5 Homo sapiens cDNA... 66 2e-08 H09529, H09529 yl95h10.s1 Homo sapiens cDNA clone 46129 3'. 66 2e-08 AA286791, AA286791 zs54h07.rl NCI\_CGAP\_GCB1 Homo sapiens cDNA... 66 2e-08 W04418, W04418 za43c06.rl Soares fetal liver spleen 1NFLS Hom... 58 4e-06 AA101045, AA101045 zm27e12.r1 Stratagene pancreas (#937208) H... 56 1e-05 AA064706, AA064706 zm13f07.r1 Stratagene pancreas (#937208) H... 42 0.22 AA810035, AA810035 od11f12.s1 NCI\_CGAP\_GCB1 Homo sapiens cDNA... 40 0.86 T41169, T41169 ya31g10.s3 Homo sapiens cDNA clone 62274 3' co... 40 0.86 AA070108, AA070108 zm69d06.s1 Stratagene neuroepithelium (#93... 40 0.86 AA706183, AA706183 ag93e01.s1 Stratagene hNT neuron (#937233)... 40 0.86 AA393069, AA393069 zt69e09.rl Soares testis NHT Homo sapiens ... 40 0.86 AA371600, AA371600 EST83650 Pituitary gland, subtracted (prol... 40 0.86 AA977820, AA977820 oq78a09.s1 NCI\_CGAP\_Kid6 Homo sapiens cDNA... 38 3.4 AA584760, AA584760 no04c06.s1 NCI\_CGAP\_Phe1 Homo sapiens cDNA... 38 3.4 AA584615, AA584615 no08g12.s1 NCI\_CGAP\_Phe1 Homo sapiens cDNA... 38 3.4 AA229827, AA229827 nc48c04.rl NCI\_CGAP\_Pr3 Homo sapiens cDNA ... 38 3.4 W21398, W21398 zb50a11.rl Soares fetal lung NbHL19W Homo sapi... 38 3.4

AA136933, AA136933 zn97f07.s1 Stratagene fetal retina 937202 ... 38 3.4

AA869501, AA869501 vq08g11.rl Barstead stromal cell line MPLR... 833 0.0 AA221749, AA221749 my28g01.rl Barstead mouse pooled organs MP... 789 0.0 AA271363, AA271363 va71d08.r1 Soares mouse 3NME12 5 Mus muscu... 781 0.0 AA544727, AA544727 vk35d01.rl Soares mouse mammary gland NbMM... 773 0.0 W84968, W84968 mf42e02.r1 Soares mouse embryo NbME13.5 14.5 M... 640 0.0 AA153324, AA153324 ms61e11.rl Stratagene mouse embryonic carc... 617 e-175 AA673899, AA673899 vo86g07.rl Barstead mouse irradiated colon... 583 e-164 AA797488, AA797488 vw28a05.rl Soares mouse mammary gland NbMM... 519 e-145 W71831, W71831 me45b06.r1 Soares mouse embryo NbME13.5 14.5 M... 472 e-131 AA213358, AA213358 mu74e04.rl Stratagene mouse embryonic carc... 444 e-123 W75918, W75918 me82f05.r1 Soares mouse embryo NbME13.5 14.5 M... 444 e-123 AA038141, AA038141 mi81e05.r1 Soares mouse p3NMF19.5 Mus musc... 359 3e-97 AA038288, AA038288 mi83b04.rl Soares mouse p3NMF19.5 Mus musc... 323 1e-86 AA017742, AA017742 mh40c03.rl Soares mouse placenta 4NbMP13.5... 297 8e-79 AA771297, AA771297 vt17g04.rl Barstead mouse myotubes MPLRB5 ... 297 8e-79 AA105228, AA105228 mp45b11.rl Barstead MPLRB1 Mus musculus cD... 295 3e-78 AA068340, AA068340 mm53f01.r1 Stratagene mouse embryonic carc... 293 1e-77 AA612347, AA612347 vo05c08.rl Stratagene mouse skin (#937313)... 281 5e-74 AA038300, AA038300 mi83d04.r1 Soares mouse p3NMF19.5 Mus musc... 270 2e-70 AA500952, AA500952 vg01h04.rl Soares mouse NbMH Mus musculus ... 252 4e-65 W08368, W08368 mb41f07.r1 Soares mouse p3NMF19.5 Mus musculus... 212 4e-53 AA052280, AA052280 ma82e12.rl Soares mouse p3NMF19.5 Mus musc... 123 3e-26 AA064466, AA064466 ml49c05.rl Stratagene mouse testis (#93730... 107 2e-21 AA271566, AA271566 vb74b09.rl Soares mouse 3NME12 5 Mus muscu... 60 3e-07 C86222, C86222 Mus musculus fertilized egg cDNA 3'-end seque... 42 0.078 W83632, W83632 mf31a04.r1 Soares mouse embryo NbME13.5 14.5 M... 42 0.078 AA423627, AA423627 ve80f01.rl Soares mouse mammary gland NbMM... 42 0.078 AA036586, AA036586 mi41h08.rl Soares mouse embryo NbME13.5 14... 42 0.078 AA207496, AA207496 mv78g02.rl GuayWoodford Beier mouse kidney... 42 0.078 AA120433, AA120433 mp82h11.r1 Soares 2NbMT Mus musculus cDNA ... 42 0.078 W08185, W08185 mb42h02.rl Soares mouse p3NMF19.5 Mus musculus... 38 1.2 AA065563, AA065563 ml71b06.rl Stratagene mouse kidney (#93731... 38 1.2 AA288756, AA288756 mr46h07.rl Life Tech mouse embryo 15 5dpc ... 38 1.2 AA119334, AA119334 mp80e10.r1 Soares 2NbMT Mus musculus cDNA ... 38 1.2 AA163051, AA163051 ms24a10.rl Stratagene mouse skin (#937313)... 38 1.2 N28074, N28074 MDB1392R Mouse brain, Stratagene Mus musculus ... 38 1.2 AA288757, AA288757 mr46h08.rl Life Tech mouse embryo 15 5dpc ... 38 1.2 AA122857, AA122857 mq06a02.r1 Soares 2NbMT Mus musculus cDNA ... 38 1.2 AA617519, AA617519 vj77d05.rl Knowles Solter mouse blastocyst... 38 1.2

w89420, w89420 misubu3.rl Soares mouse embryo NbME13.5 14.5 M 38 1.2
AI047837, AI047837 ud64c11.x1 Sugano mouse liver mlia Mus mus 38 1.2
AA840310, AA840310 vw91a10.r1 Stratagene mouse skin (#937313) 36 4.8
AA986428, AA986428 ue13b04.x1 Sugano mouse embryo mewa Mus mu 36 4.8
W47677, W47677 mc89g07.rl Soares mouse embryo NbME13.5 14.5 M 36 4.8
AA057996, AA057996 mj56c10.rl Soares mouse embryo NbME13.5 14 36 4.8
AA183858, AA183858 mo95h01.r1 Stratagene mouse testis (#93730 36 4.8
AA212232, AA212232 mu43e08.rl Soares 2NbMT Mus musculus cDNA 36 4.8
W41067, W41067 mc39a06.r1 Soares mouse p3NMF19.5 Mus musculus 36 4.8
AA967594, AA967594 uh01d06.rl Soares mouse hypothalamus NMHy 36 4.8
AA414093, AA414093 vc64c07.s1 Knowles Solter mouse 2 cell Mus 36 4.8
AA123833, AA123833 mp93c03.r1 Soares 2NbMT Mus musculus cDNA 36 4.8
AA432920, AA432920 vd91b11.rl Soares mouse NbMH Mus musculus 36 4.8
AA874496, AA874496 vx03a08.rl Soares 2NbMT Mus musculus cDNA 36 4.8
AA000433, AA000433 me76e09.rl Soares mouse embryo NbME13.5 14 36 4.8
AA023983, AA023983 mh94a07.rl Soares mouse placenta 4NbMP13.5 36 4.8
AA013726, AA013726 mh12e09.r1 Soares mouse placenta 4NbMP13.5 36 4.8
AA274648, AA274648 vb08c01.rl Soares mouse NML Mus musculus c 36 4.8
AA140347, AA140347 mq89g06.r1 Stratagene mouse heart (#937316 36 4.8
AA499377, AA499377 vi89c07.r1 Stratagene mouse heart (#937316 36 4.8
C88747, C88747 Mus musculus early blastocyst cDNA, clone 01B 36 4.8
AA726125, AA726125 vu88c06.rl Stratagene mouse skin (#937313) 36 4.8
AA760311, AA760311 vv71c12.r1 Stratagene mouse skin (#937313) 36 4.8
AA763007, AA763007 vw60b05.rl Soares mouse mammary gland NMLM 36 4.8
AA929878, AA929878 vz44d03.rl Soares 2NbMT Mus musculus cDNA 36 4.8
W59064, W59064 md67e10.rl Soares mouse embryo NbME13.5 14.5 M 36 4.8
AA103519, AA103519 mo24b12.rl Life Tech mouse embryo 13 5dpc 36 4.8
AA222310, AA222310 my14d08.rl Barstead mouse heart MPLRB3 Mus 36 4.8
W83557, W83557 mf32d02.r1 Soares mouse embryo NbME13.5 14.5 M 36 4.8
AA168631, AA168631 ms33c05.rl Stratagene mouse skin (#937313) 36 4.8
AA960143, AA960143 vw60b05.s1 Soares mouse mammary gland NMLM 36 4.8
W34557, W34557 mc58a05.r1 Soares mouse embryo NbME13.5 14.5 M 36 4.8
W98818, W98818 mf94e06.r1 Soares mouse embryo NbME13.5 14.5 M 36 4.8
AA008527, AA008527 mg85h01.r1 Soares mouse embryo NbME13.5 14 36 4.8
AA008734, AA008734 mg86h03.rl Soares mouse embryo NbME13.5 14 36 4.8
AA510568, AA510568 vg33a10.rl Soares mouse mammary gland NbMM 36 4.8
AA672524, AA672524 vo59e11.rl Soares mouse mammary gland NbMM 36 4.8
AA052773, AA052773 mf24h01.rl Soares mouse embryo NbME13.5 14 36 4.8
AA096626, AA096626 mo09h06.rl Life Tech mouse embryo 10 5dpc 36 4.8
AA124880, AA124880 mp73e06.rl Soares 2NbMT Mus musculus cDNA 36 4.8
AA198005, AA198005 mv12b09.rl GuayWoodford Beier mouse kidney 36 4.8
AA624213, AA624213 vm98h06.rl Knowles Solter mouse blastocyst 36 4.8
AA521863, AA521863 vi08b01.rl Barstead mouse myotubes MPLRB5 36 4.8
AA692113, AA692113 vt19d03.rl Barstead mouse myotubes MPLRB5 36 4.8
W71551, W71551 me39e11.rl Soares mouse embryo NbME13.5 14.5 M. 36 4 8

AA646501, AA646501 vn12g12.r1 Stratagene mouse heart (#937316... 36 4.8 AA607056, AA607056 vm95e05.rl Knowles Solter mouse blastocyst... 36 4.8 AA163340, AA163340 ms65b10.rl Stratagene mouse embryonic carc... 36 4.8 AA110893, AA110893 mm02b04.r1 Stratagene mouse kidney (#93731... 36 4.8 AI030290, AI030290 UI-R-C0-jb-d-01-0-UI.s1 UI-R-C0 Rattus nor... 293 1e-77 C71833, C71833 Rice cDNA, partial sequence (E0428 1A) 44 0.017 AA926551, AA926551 TENS1173 T. cruzi epimastigote normalized ... 42 0.069 AA875699, AA875699 TENU0170 T.cruzi epimastigote normalized c... 42 0.069 AA567661, AA567661 HL01595.5prime HL Drosophila melanogaster ... 40 0.27 C74504, C74504 Rice cDNA, partial sequence (E31753 1A) 40 0.27 AA698333, AA698333 HL04291.5prime HL Drosophila melanogaster ... 38 1.1 AA441429, AA441429 LD16359.5prime LD Drosophila melanogaster ... 38 1.1 N68770, N68770 TgESTzy35b12.rl TgRH Tachyzoite cDNA Toxoplasm... 38 1.1 AA246440, AA246440 LD05311.5prime LD Drosophila melanogaster ... 38 1.1 AA801776, AA801776 GM12975.5prime GM Drosophila melanogaster ... 38 1.1 N69148, N69148 TgESTzy33d10.rl TgRH Tachyzoite cDNA Toxoplasm... 38 1.1 AA536484, AA536484 LD17114.5prime LD Drosophila melanogaster ... 38 1.1 AA392544, AA392544 LD11451.5prime LD Drosophila melanogaster ... AA202696, AA202696 LD03182.5prime LD Drosophila melanogaster ... AA392367, AA392367 LD11287.5prime LD Drosophila melanogaster ... AA264629, AA264629 LD08245.5prime LD Drosophila melanogaster ... 38 1.1 AA735318, AA735318 LD21104.5prime LD Drosophila melanogaster ... 38 1.1 AA264558, AA264558 LD08333.5prime LD Drosophila melanogaster ... AA536476, AA536476 LD17106.5prime LD Drosophila Embryo Drosop... 38 1.1 AA957774, AA957774 UI-R-E1-fv-f-04-0-UI.s1 UI-R-E1 Rattus nor... 38 1.1 AA567991, AA567991 HL02092.5prime HL Drosophila melanogaster ... 38 1.1 AA957876, AA957876 UI-R-E1-fv-f-04-0-UI.s2 UI-R-E1 Rattus nor... 38 1.1 AA892488, AA892488 EST196291 Normalized rat kidney, Bento Soa... 38 1.1 AA699001, AA699001 HL06668.5prime HL Drosophila melanogaster ... 36 4.3 C19706, C19706 Rice cDNA, partial sequence (E10809 1A) 36 4.3 D41773, RICS4574A Rice cDNA, partial sequence (S4574 2A). 36 4.3 C40680, C40680 C.elegans cDNA clone yk247c4: 5' end, single... 36 4.3 AA698625, AA698625 HL05354.5prime HL Drosophila melanogaster ... C82819, C82819 Oryctolagus cuniculus corneal endothelial cDN... 36 4.3 D46016, RICS10393A Rice cDNA, partial sequence (S10393 3A). 36 4.3 AA536314, AA536314 LD16858.5prime LD Drosophila melanogaster ... 36 4.3 AA801012, AA801012 EST190509 Normalized rat muscle, Bento Soa... 36 4.3 D46541, RICS11289A Rice cDNA, partial sequence (S11289 1A). 36 4.3 D47315, RICS12612A Rice cDNA, partial sequence (S12612 1A). 36 4.3 AA735857, AA735857 GM09977.5prime GM Drosophila melanogaster ... 36 4.3 AA753921, AA753921 97BS0370 Rice Immature Seed Lambda ZAPII c... 36 4.3 D47243, RICS12505A Rice cDNA, partial sequence (S12505 1A). AA978395, AA978395 LD28411.5prime LD Drosophila melanogaster ... 36 4.3

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D15134, RICC0136A Rice cDNA, partial sequence (C0136A).	36 4.3
D46483, RICS11185A Rice cDNA, partial sequence (S11185_1A).	36 4.3
D46618, RICS11395A Rice cDNA, partial sequence (S11395_1A).	36 4.3
D46659, RICS11457A Rice cDNA, partial sequence (S11457_1A).	36 4.3
D46719, RICS11572A Rice cDNA, partial sequence (S11572_1A).	36 4.3
D48579, RICS14880A Rice cDNA, partial sequence (S14880_2A).	36 4.3
AA802334, AA802334 GM04219.5prime GM Drosophila melanoga	ster 36 4.3
D46066, RICS10470A Rice cDNA, partial sequence (S10470_1A).	36 4.3
D47037, RICS12104A Rice cDNA, partial sequence (S12104_1A).	36 4.3
D46874, RICS11807A Rice cDNA, partial sequence (S11807_2A).	36 4.3
D47174, RICS12340A Rice cDNA, partial sequence (S12340_2A).	36 4.3
T04578, T04578 625 Lambda-PRL2 Arabidopsis thaliana cDNA clo	n 36 4.3
C83675, C83675 Oryctolagus cuniculus corneal endothelial cDN	36 4.3
D47950, RICS13762A Rice cDNA, partial sequence (S13762_1A).	36 4.3
R90044, R90044 16399 Lambda-PRL2 Arabidopsis thaliana cDNA	cl 36 4.3
D46994, RICS12013A Rice cDNA, partial sequence (S12013 2A).	36 4.3
AA440820, AA440820 LD15713.5prime LD Drosophila melanogasi	ter 36 4.3
	36 4.3
Z84004, SSZ84004 S.scrofa mRNA; expressed sequence tag (5';	36 4.3
D47519, RICS13070A Rice cDNA, partial sequence (S13070_1A).	36 4.3
C19735, C19735 Rice cDNA, partial sequence (E10858_1A)	36 4.3
D47231, RICS12462A Rice cDNA, partial sequence (S12462_1A).	36 4.3
D47147, RICS12293A Rice cDNA, partial sequence (S12293_1A).	36 4.3
AA950198, AA950198 LD30147.5prime LD Drosophila melanogasi	ter 36 4.3
Z47624, ATTS4480 A. thaliana transcribed sequence; clone TAI	36 4.3
D45955, RICS10259A Rice cDNA, partial sequence (S10259_1A).	36 4.3
D47137, RICS12280A Rice cDNA, partial sequence (S12280_1A).	36 4.3
D69927, CELK093H2F C.elegans cDNA clone yk93h2: 5' end, sin	
AA392275, AA392275 LD11117.5prime LD Drosophila melanogasi	ter 36 4.3

### SEQ ID NO:546

D87455, D87455 Human mRNA for KIAA0266 gene, complete cds Z99129, HS425C14 Human DNA sequence from clone 425C14 on chr... 42 0.20 D90900, D90900 Synechocystis sp. PCC6803 complete genome, 2/... 40 0.80 Z74281, SCYDL233W S.cerevisiae chromosome IV reading frame O... 38 3.1 AL021528, HS394P21 Homo sapiens DNA sequence from PAC 394P21... 38 3.1 Z49155, HSL83D3 Human DNA from cosmid L83d3, Huntington's Di... 38 3.1 U33761, HSU33761 Human cyclin A/CDK2-associated p45 (Skp2) mR... 38 3.1 AF052832, AF052832 Trypanosoma cruzi CL Brener cosmid 1b21 ch... 38 3.1 Z98600, SPAC20G4 S.pombe chromosome I cosmid c20G4 38 3.1

Y09438, SPHUSPLUS S.pombe hus1+ gene 38 3.1 D29951, MUSKIF Mouse mRNA for kinesin family protein KIF1a, ... 38 3.1

#### **HUMAN ESTs**

AA151187, AA151187 zo03c11.r1 Stratagene colon (#937204) Homo... 694 0.0 AA824593, AA824593 oc83d10.s1 NCI\_CGAP\_GCB1 Homo sapiens cDNA... 670 0.0 AA954862, AA954862 op20c03.s1 NCI\_CGAP\_Co12 Homo sapiens cDNA... 581 e-164 T16360, T16360 NIB1193 Normalized infant brain, Bento Soares ... 517 e-145 R54592, R54592 yg81h10.s1 Homo sapiens cDNA clone 40102 3'. 511 e-143 AA373594, AA373594 EST85631 HSC172 cells I Homo sapiens cDNA ... 507 e-142 AA100660, AA100660 zl90a05.r1 Stratagene colon (#937204) Homo... 383 e-104 R42009, R42009 yg05b04.s1 Homo sapiens cDNA clone 31336 3'. 379 e-103 AA249614, AA249614 k3041.seq.F Human fetal heart, Lambda ZAP ... 252 5e-65 AA360633, AA360633 EST69800 T-cell lymphoma Homo sapiens cDNA... 182 4e-44 AA053498, AA053498 zl70b11.r1 Stratagene colon (#937204) Homo... 38 1.5 AA992442, AA992442 or85h03.s1 NCI\_CGAP\_Lu5 Homo sapiens cDNA ... 38 1.5

AA065677, AA065677 mm43c03.rl Stratagene mouse melanoma (#937... 297 4e-79 AA529728, AA529728 vi38g12.rl Beddington mouse embryonic regi... 42 0.035 W91608, W91608 MTA.D10.092.A MTA adult mouse thymus library M... 42 0.035 AA177186, AA177186 mt51a11.rl Stratagene mouse embryonic carc... 42 0.035 AA048008, AA048008 mj26h10.rl Soares mouse embryo NbME13.5 14... 36 2.2 AA637535, AA637535 vu10c02.rl Barstead mouse myotubes MPLRB5 ... 36 2.2 AA726355, AA726355 vu90c09.rl Stratagene mouse skin (#937313)... 36 2.2 AA404025, AA404025 va31c11.rl GuayWoodford Beier mouse kidney... 36 2.2 AA660014, AA060014 ml34d07.rl Stratagene mouse testis (#93730... 36 2.2 AA870617, AA870617 vq23h10.rl Barstead stromal cell line MPLR... 36 2.2 AA414112, AA414112 vc64f08.sl Knowles Solter mouse 2 cell Mus... 36 2.2 AA764250, AA764250 vv49e09.rl Soares 2NbMT Mus musculus cDNA ... 36 2.2

H34350, H34350 EST111226 Rat PC-12 cells, NGF-treated (9 days... 36 1.9 C40718, C40718 C.elegans cDNA clone yk247f9 : 5' end, single... 36 1.9 AA817925, AA817925 UI-R-A0-af-g-04-0-UI.s1 UI-R-A0 Rattus nor... 36 1.9 AA955650, AA955650 UI-R-E1-fc-e-10-0-UI.s1 UI-R-E1 Rattus nor... 36 1.9

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U66201, MMU66201 Mus musculus fibroblast growth factor homolo... 42 0.35
U66197, HSU66197 Human fibroblast growth factor homologous fa... 42 0.35
AF020738, AF020738 Mus musculus fibroblast growth factor-rela... 42 0.35
U85773, HSU85773 Human phosphomannomutase (PMM2) mRNA, comple... 40 1.4
Z46966, MMIMOGN44 M.musculus mRNA for imogen 44. 40 1.4
AC004301, AC004301 Drosophila melanogaster DNA sequence (P1 D... 40 1.4
U86662, LEU86662 Lycopersicon esculentum VPS41 (tVPS41) mRNA,... 40 1.4

#### **HUMAN ESTs**

W22160, W22160 63A6 Human retina cDNA Tsp509I-cleaved sublibr... 791 0.0 AA860926, AA860926 ak22d06.s1 Soares testis NHT Homo sapiens ... 650 0.0 AA348243, AA348243 EST54707 Hippocampus I Homo sapiens cDNA 5... 513 e-143 AA551799, AA551799 nk04a11.s1 NCI\_CGAP\_Co2 Homo sapiens cDNA ... 363 4e-98 AA327309, AA327309 EST30621 Colon I Homo sapiens cDNA 5' end AA344913, AA344913 EST50856 Gall bladder II Homo sapiens cDNA... 337 2e-90 AA121174, AA121174 zl88g08.s1 Stratagene colon (#937204) Homo... 317 2e-84 AA121198, AA121198 zl88g08.rl Stratagene colon (#937204) Homo... 317 2e-84 AA001561, AA001561 ze46e07.s1 Soares retina N2b4HR Homo sapie... 42 0.17 AA888147, AA888147 04h11.sl NCI\_CGAP\_Co10 Homo sapiens cDNA... 40 0.67 AA946650, AA946650 oq38h09.s1 NCI\_CGAP\_Kid5 Homo sapiens cDNA... 40 0.67 AA435587, AA435587 zt85d07.s1 Soares testis NHT Homo sapiens ... 40 0.67 AA806381, AA806381 oc22g05.s1 NCI\_CGAP\_GCB1 Homo sapiens cDNA... 40 0.67 AA577174, AA577174 nm86e11.s1 NCI CGAP Co9 Homo sapiens cDNA ... 40 0.67 AA215903, AA215903 hp0042.seq.F Fetal heart, Lambda ZAP Expre... 40 0.67 AA262229, AA262229 zs25b12.s1 NCI\_CGAP\_GCB1 Homo sapiens cDNA... 40 0.67 AA969632, AA969632 op38h05.s1 Soares\_NFL\_T\_GBC S1 Homo sapien... 40 0.67 N35888, N35888 yy28b05.s1 Homo sapiens cDNA clone 272529 3'. AI005324, AI005324 ou13h07.x1 Soares\_NFL\_T\_GBC\_S1 Homo sapien... 40 0.67 AA172158, AA172158 zp29a01.s1 Stratagene neuroepithelium (#93... 40 0.67 AA860208, AA860208 ak48c10.s1 Soares testis NHT Homo sapiens ... 40 0.67 AA814296, AA814296 nz07d08.s1 NCI\_CGAP\_GCB1 Homo sapiens cDNA... 40 0.67 AA873216, AA873216 oh70f04.s1 NCI CGAP Kid5 Homo sapiens cDNA... 40 0.67 AA403143, AA403143 zv66d01.r1 Soares total fetus Nb2HF8 9w Ho... 40 0.67 W45005, W45005 zc05c12.rl Soares parathyroid tumor NbHPA Homo... 40 0.67 W32428, W32428 zc05c12.s1 Soares parathyroid tumor NbHPA Homo... 40 0.67 AA974988, AA974988 on59b06.s1 Soares\_NFL\_T GBC S1 Homo sapien... 40 0.67 AA725024, AA725024 ah97h10.s1 Soares NFL T GBC S1 Homo sapien... 40 0.67 AA757360, AA757360 ah98a01.s1 Soares NFL T GBC S1 Homo sapien... 40 0.67 N72025, N72025 yz96g02.s1 Homo sapiens cDNA clone 290930 3'. 40 0.67 R02514, R02514 ye70b08.rl Homo sapiens cDNA clone 123063 5'. 40 0.67 AA039536, AA039536 zk39h10.s1 Soares pregnant uterus NbHPU Ho... 40 0.67 AA877455, AA877455 ob33g01.s1 NCI\_CGAP\_Kid5 Homo sapiens cDNA... 40 0.67 AA041240, AA041240 zf07g05.rl Soares fetal heart NbHH19W Homo... 40 0.67

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N35076, N35076 yy19b08.s1 Homo sapiens cDNA clone 271671 3'.
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H30248, H30248 yp42a01.s1 Homo sapiens cDNA clone 190056 3'.
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R82551, R82551 yi19d06.r1 Homo sapiens cDNA clone 149195 5'.
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AI047609, AI047609 uh63g07.rl Soares mouse embryonic stem cel... 36 3.7 AA692425, AA692425 vt59b05.rl Barstead mouse irradiated colon... 36 3.7 AA966976, AA966976 ua38f11.r1 Soares mouse mammary gland NbMM... 36 3.7 AA856298, AA856298 vw99b01.rl Soares 2NbMT Mus musculus cDNA ... 36 3.7 W20935, W20935 mb96c07.r1 Soares mouse p3NMF19.5 Mus musculus... 36 3.7 AA230661, AA230661 mw15f08.r1 Soares mouse 3NME12 5 Mus muscu... 36 3.7 AA111190, AA111190 mp66b11.rl Soares 2NbMT Mus musculus cDNA ... 36 3.7 AA840087, AA840087 uc99h12.rl Soares mouse uterus NMPu Mus mu... 36 3.7 AA089210, AA089210 mo05d10.rl Stratagene mouse lung 937302 Mu... 36 3.7 AI035925, AI035925 ub49e05.rl Soares mouse mammary gland NbMM... 36 3.7 AA824205, AA824205 vy20g08.rl Stratagene mouse macrophage (#9... 36 3.7 AA793845, AA793845 vr35e12.rl Barstead mouse myotubes MPLRB5 ... AA239210, AA239210 mx89e02.rl Soares mouse NML Mus musculus c... 36 3.7 AA711873, AA711873 vu28e06.r1 Barstead mouse myotubes MPLRB5 ... 36 3.7 AA645119, AA645119 vs72d03.r1 Stratagene mouse skin (#937313)... 36 3.7

AA957268, AA957268 UI-R-E1-fq-e-06-0-UI.s1 UI-R-E1 Rattus nor... C83463, C83463 Oryctolagus cuniculus corneal endothelial cDN... 38 0.84 AA859448, AA859448 UI-R-A0-bf-b-01-0-UI.s1 UI-R-A0 Rattus nor... 38 0.84 AA874930, AA874930 UI-R-E0-ci-b-05-0-UI.s1 UI-R-E0 Rattus nor... C82607, C82607 Oryctolagus cuniculus corneal endothelial cDN... 38 0.84 AI009631, AI009631 EST204082 Normalized rat lung, Bento Soare... 38 0.84 AA801145, AA801145 EST190642 Normalized rat ovary, Bento Soar... AI012760, AI012760 EST207211 Normalized rat placenta, Bento S... 38 0.84 AA956139, AA956139 UI-R-E1-fi-h-08-0-UI.s1 UI-R-E1 Rattus nor... 38 0.84 AA801144, AA801144 EST190641 Normalized rat ovary, Bento Soar... 38 0.84 AA660819, AA660819 00713 MtRHE Medicago truncatula cDNA 5' 38 0.84 AA859865, AA859865 UI-R-E0-cc-b-04-0-UI.s1 UI-R-E0 Rattus nor... 38 0.84 AI009035, AI009035 EST203486 Normalized rat embryo, Bento Soa... AA859542, AA859542 UI-R-E0-br-d-03-0-UI.s1 UI-R-E0 Rattus nor... 38 0.84 T00613, T00613 wEST01334 Caenorhabditis elegans cDNA clone CE... 38 0.84 H32878, H32878 EST108396 Rat PC-12 cells, untreated Rattus sp... 36 3.3 AA125602, AA125602 JM00M011.QM3 Miracidia Sjc 3/96 Schistosom... 36 3.3 D45997, RICS10346A Rice cDNA, partial sequence (S10346 1A). 36 3.3 AA943364, AA943364 EST198863 Normalized rat brain, Bento Soar... 36 3.3 C68472, C68472 C.elegans cDNA clone yk305a12: 5' end, singl... 36 3.3 AA785775, AA785775 h4b05a1.fl Aspergillus nidulans 24hr asexu... 36 3.3 D46069, RICS10475A Rice cDNA, partial sequence (S10475 1A). 36 3.3 AA660859, AA660859 00754 MtRHE Medicago truncatula cDNA 5' si... 36 3.3 Z33974, ATTS3035 A. thaliana transcribed sequence; clone PAP... 36 3.3 Z32603, ATTS2731 A. thaliana transcribed sequence; clone PAP... 36 3.3 AA955567, AA955567 UI-R-E1-fa-a-08-0-UI.s1 UI-R-E1 Rattus nor... 36 3.3 AA842765, AA842765 M-EST080 Sugarcane mature stalk Saccharum ... 36 3.3 Z32602, ATTS2730 A. thaliana transcribed sequence; clone PAP... 36 3.3

# **SEQ ID NO:548**

U66197, HSU66197 Human fibroblast growth factor homologous fa... 42 0.34
AF020738, AF020738 Mus musculus fibroblast growth factor-rela... 42 0.34
U66201, MMU66201 Mus musculus fibroblast growth factor homolo... 42 0.34
Z46966, MMIMOGN44 M.musculus mRNA for imogen 44. 40 1.3
AC004301, AC004301 Drosophila melanogaster DNA sequence (P1 D... 40 1.3
U86662, LEU86662 Lycopersicon esculentum VPS41 (tVPS41) mRNA,... 40 1.3
U85773, HSU85773 Human phosphomannomutase (PMM2) mRNA, comple... 40 1.3

#### **HUMAN ESTs**

W22160, W22160 63A6 Human retina cDNA Tsp509I-cleaved sublibr... 791 0.0 AA860926, AA860926 ak22d06.s1 Soares testis NHT Homo sapiens ... 650 0.0 AA348243, AA348243 EST54707 Hippocampus I Homo sapiens cDNA 5... 513 e-143 AA551799, AA551799 nk04a11.s1 NCI\_CGAP\_Co2 Homo sapiens cDNA ... 363 3e-98 AA327309, AA327309 EST30621 Colon I Homo sapiens cDNA 5' end 353 3e-95 AA344913, AA344913 EST50856 Gall bladder II Homo sapiens cDNA... 337 2e-90 AA121198, AA121198 zl88g08.rl Stratagene colon (#937204) Homo... 317 2e-84 AA121174, AA121174 zl88g08.s1 Stratagene colon (#937204) Homo... 317 2e-84 AA001561, AA001561 ze46e07.s1 Soares retina N2b4HR Homo sapie... 42 0.16 AA041240, AA041240 zf07g05.r1 Soares fetal heart NbHH19W Homo... 40 0.64 AA039536, AA039536 zk39h10.s1 Soares pregnant uterus NbHPU Ho... 40 0.64 AA040802, AA040802 zf07g05.s1 Soares fetal heart NbHH19W Homo... 40 0.64 AA573297, AA573297 nk98d09.s1 NCI\_CGAP\_Co3 Homo sapiens cDNA ... 40 0.64 N35888, N35888 yy28b05.s1 Homo sapiens cDNA clone 272529 3'. 40 0.64 AA888147, AA888147 04h11.sl NCI\_CGAP\_Co10 Homo sapiens cDNA... 40 0.64 AA172158, AA172158 zp29a01.s1 Stratagene neuroepithelium (#93... 40 0.64 AA877455, AA877455 ob33g01.s1 NCI\_CGAP\_Kid5 Homo sapiens cDNA... 40 0.64 R02514, R02514 ye70b08.rl Homo sapiens cDNA clone 123063 5'. 40 0.64 AA514777, AA514777 ni24b01.s1 NCI\_CGAP\_Co4 Homo sapiens cDNA ... 40 0.64 AA416734, AA416734 zu08c01.s1 Soares testis NHT Homo sapiens ... 38 2.5 N98472, N98472 yy65a04.rl Homo sapiens cDNA clone 278382 5'. AA416815, AA416815 zu08c01.rl Soares testis NHT Homo sapiens ... 38 2.5 AA431486, AA431486 zw72g01.s1 Soares testis NHT Homo sapiens ... 38 2.5 AA948291, AA948291 oq34d02.s1 NCI\_CGAP\_GC4 Homo sapiens cDNA ... 38 2.5 AA852281, AA852281 NHTBCael1g05rl Normal Human Trabecular Bon... 38 2.5

AA616807, AA616807 vn68c05.rl Barstead mouse irradiated colon... 180 1e-43 AA469884, AA469884 vf71g10.rl Barstead mouse pooled organs MP... 40 0.23 AA230758, AA230758 my32g10.r1 Barstead mouse pooled organs MP... 40 0.23 AA038869, AA038869 mi95b10.rl Soares mouse p3NMF19.5 Mus musc... 40 0.23 AA763419, AA763419 vw54a12.rl Soares mouse mammary gland NMLM... 40 0.23 AA185487, AA185487 mt62c07.r1 Soares 2NbMT Mus musculus cDNA ... 40 0.23 AA106439, AA106439 ml59a08.rl Stratagene mouse testis (#93730... 40 0.23 AA276740, AA276740 vc42a12.rl Soares mouse 3NbMS Mus musculus... 40 0.23 AA068686, AA068686 mm59a03.rl Stratagene mouse embryonic carc... 38 0.91 AA711873, AA711873 vu28e06.rl Barstead mouse myotubes MPLRB5 ... 36 3.6 AA856298, AA856298 vw99b01.rl Soares 2NbMT Mus musculus cDNA ... W20935, W20935 mb96c07.r1 Soares mouse p3NMF19.5 Mus musculus... 36 3.6 AA966976, AA966976 ua38f11.r1 Soares mouse mammary gland NbMM... 36 3.6 AA921560, AA921560 vy52c06.rl Stratagene mouse lung 937302 Mu... 36 3.6 AA692425, AA692425 vt59b05.rl Barstead mouse irradiated colon... 36 3.6 W87202, W87202 mf55g08.rl Soares mouse embryo NbME13.5 14.5 M... 36 3.6 AA840087, AA840087 uc99h12.r1 Soares mouse uterus NMPu Mus mu... 36 3.6 AA111190, AA111190 mp66b11.rl Soares 2NbMT Mus musculus cDNA ... 36 3.6 AA239210, AA239210 mx89e02.rl Soares mouse NML Mus musculus c... 36 3.6 AA793845, AA793845 vr35e12.rl Barstead mouse myotubes MPLRB5 ... 36 3.6 AA645119, AA645119 vs72d03.rl Stratagene mouse skin (#937313)... 36 3.6 AA230661, AA230661 mw15f08.r1 Soares mouse 3NME12 5 Mus muscu... 36 3.6 AA824205, AA824205 vy20g08.r1 Stratagene mouse macrophage (#9... 36 3.6 C87249, C87249 Mus musculus fertilized egg cDNA 3'-end seque... 36 3.6 AA967316, AA967316 vj47a03.rl Stratagene mouse skin (#937313)... 36 3.6 AA591243, AA591243 vm18c04.r1 Knowles Solter mouse blastocyst... 36 3.6 AI035925, AI035925 ub49e05.rl Soares mouse mammary gland NbMM... 36 3.6 AA530735, AA530735 vj32g11.r1 Stratagene mouse diaphragm (#93... 36 3.6 AA218431, AA218431 my07e05.rl Barstead mouse lung MPLRB2 Mus ... 36 3.6 W62989, W62989 md88h12.rl Soares mouse embryo NbME13.5 14.5 M... 36 3.6 AA089210, AA089210 mo05d10.r1 Stratagene mouse lung 937302 Mu... 36 3.6 AA796056, AA796056 vo65d01.rl Soares mouse mammary gland NbMM... 36 3.6 AA542324, AA542324 vk53e07.r1 Stratagene mouse Tcell 937311 M... 36 3.6

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D45997, RICS10346A Rice cDNA, partial sequence (S10346\_1A). 36 3.2 Z32603, ATTS2731 A. thaliana transcribed sequence; clone PAP... 36 3.2 AA785775, AA785775 h4b05a1.fl Aspergillus nidulans 24hr asexu... 36 3.2 C68472, C68472 C.elegans cDNA clone yk305a12 : 5' end, singl... 36 3.2 AA125602, AA125602 JM00M011.QM3 Miracidia Sjc 3/96 Schistosom... 36 3.2 AA943364, AA943364 EST198863 Normalized rat brain, Bento Soar... 36 3.2 Z32602, ATTS2730 A. thaliana transcribed sequence; clone PAP... 36 3.2

#### SEQ ID NO:549

U79271, HSU79271 Human clones 23920 and 23921 mRNA sequence 650 0.0 AC000395, AC000395 Genomic sequence from Human 9q34, complete... 42 0.28 AC004636, AC004636 Homo sapiens chromosome 5, P1 clone 1268h6... 42 0.28 M94579, HUMCEL Human carboxyl ester lipase (CEL) gene, comple... 42 0.28 AC002097, AC002097 Homo sapiens chromosome 9q34, clone 246H5,... AB006709, AB006709 Vibrio alginolyticus rpoN gene for RNA po... 42 0.28 Z47074, CEK07C10 Caenorhabditis elegans cosmid K07C10, compl... 40 1.1 AC004755, AC004755 Homo sapiens chromosome 19, fosmid 37502, ... 40 1.1 Z28051, SCYKL051W S.cerevisiae chromosome XI reading frame O... 40 1.1 AF022655, AF022655 Homo sapiens cep250 centrosome associated ... 40 1.1 AB006708, AB006708 Arabidopsis thaliana genomic DNA, chromos... 40 1.1 AF049105, AF049105 Homo sapiens centrosomal Nek2-associated p... Z28050, SCYKL050C S.cerevisiae chromosome XI reading frame O... 40 1.1 X75781, SCXI286K S.cerevisiae chromosome XI (28.6 kb) DNA fo... 40 1.1 Y16899, DMY16899 Drosophila melanogaster mRNA for optomotor-... 38 4.3 M87854, RATBARK1 Rattus norvegicus beta-adrenergic receptor k... 38 4.3 M74822, RATMHTLL Rat MHC class I TL-like protein gene, comple... 38 4.3 M80776, HUMBARK1A Human beta-adrenergic receptor kinase 1 mRN... D84549, YSACA Candida tropicalis DNA for carnitine acetyltra... L23127, RATRMCI Rattus norvegicus germline MHC class I gene, ... 38 4.3 AC004257, AC004257 Homo sapiens chromosome 19, cosmid R33209,... U70850, CELF28F9 Caenorhabditis elegans cosmid F28F9 38 4.3 U88309, CELT23B3 Caenorhabditis elegans cosmid T23B3 38 4.3 X53421, DVCHOS18 D. virilis s18, s15, s19, s16 chorion prote... 38 4.3 D89245, D89245 Schizosaccharomyces pombe mRNA, partial cds, ... 38 4.3 AF009623, AF009623 Parascaris univalens PUMA1 (puma1) mRNA, c... 38 4.3 S48813, S48813 beta-adrenergic receptor kinase [rats, brain, ... 38 4.3 Z67883, CEK02A4 Caenorhabditis elegans cosmid K02A4, complet... 38 4.3 U90567, GGU90567 Gallus gallus glutamine rich protein mRNA, p... 38 4.3 M98498, BOVEZRINA Bos taurus ezrin mRNA, complete cds. M34073, MUSMHT10C Mus musculus (clone T10-c) MHC class I cell... 38 4.3

S81843, S81843 beta-adrenergic receptor kinase 1 [Syrian hams... 38 4.3 X61157, HSBARK H.sapiens mRNA for beta-adrenergic receptor k... 38 4.3 U08438, HSNBARKS4 Human beta-adrenergic receptor kinase (ADRB... 38 4.3 U39674, CELC06E2 Caenorhabditis elegans cosmid C06E2. 38 4.3

#### **HUMAN ESTs**

W29097, W29097 56d11 Human retina cDNA randomly primed sublib... 1045 0.0 AA886109, AA886109 ny44f05.s1 NCI\_CGAP\_Pr12 Homo sapiens cDNA... 656 0.0 AA829894, AA829894 oe51e12.s1 NCI\_CGAP\_Lu5 Homo sapiens cDNA ... 650 0.0 AA879456, AA879456 oj91g03.s1 Soares\_NFL\_T\_GBC\_S1 Homo sapien... 650 0.0 AA029201, AA029201 zk12f08.s1 Soares pregnant uterus NbHPU Ho... 650 0.0 AA102109, AA102109 zk87g11.s1 Soares pregnant uterus NbHPU Ho... 650 0.0 AA843811, AA843811 ak09c08.s1 Soares parathyroid tumor NbHPA ... 650 0.0 W72147, W72147 zd70f08.s1 Soares fetal heart NbHH19W Homo sap... 650 0.0 N51485, N51485 yz04e06.s1 Homo sapiens cDNA clone 282082 3'. 650 0.0 AI033069, AI033069 ow93f02.sl Soares\_fetal liver\_spleen 1NFLS... 642 0.0 AA161465, AA161465 zo73a06.s1 Stratagene pancreas (#937208) H... 638 0.0 N51277, N51277 yz14d07.s1 Homo sapiens cDNA clone 283021 3'. 636 e-180 N64528, N64528 yz91e06.s1 Homo sapiens cDNA clone 290434 3'. 636 e-180 H99906, H99906 yx32h10.s1 Homo sapiens cDNA clone 263491 3'. 636 e-180 AA812519, AA812519 ai79b03.s1 Soares testis NHT Homo sapiens ... 636 e-180 R71679, R71679 yi85e08.s1 Homo sapiens cDNA clone 155558 3'. 628 e-178 AA744290, AA744290 ny51d02.s1 NCI\_CGAP\_Pr18 Homo sapiens cDNA... 626 e-177 AI038590, AI038590 ox34e03.s1 Soares\_total\_fetus\_Nb2HF8\_9w Ho... 624 e-177 AA099913, AA099913 zk87g11.rl Soares pregnant uterus NbHPU Ho... 624 e-177 AA083859, AA083859 zn16d06.s1 Stratagene neuroepithelium NT2R... 622 e-176 AA883684, AA883684 al58a05.s1 Soares NFL T GBC S1 Homo sapien... 613 e-173 R39448, R39448 yc95d03.s1 Homo sapiens cDNA clone 23921 3'. 593 e-167 R36854, R36854 yf52c07.s1 Homo sapiens cDNA clone 25899 3'. 591 e-167 H98684, H98684 yx17g01.s1 Homo sapiens cDNA clone 262032 3'. 585 e-165 R07471, R07471 ye97a06.s1 Homo sapiens cDNA clone 125650 3'. 581 e-164 AA910762, AA910762 ol25h06.s1 Soares\_NFL T\_GBC\_S1 Homo sapien... 559 e-157 AA083954, AA083954 zn17d06.s1 Stratagene neuroepithelium NT2R... 555 e-156 AA346369, AA346369 EST52776 Fetal heart II Homo sapiens cDNA ... 545 e-153 R54092, R54092 yg98d07.s1 Homo sapiens cDNA clone 41818 3'. 539 e-151 H09074, H09074 yl97a06.s1 Homo sapiens cDNA clone 46164 3'. 535 e-150 N21975, N21975 yw30c10.s1 Homo sapiens cDNA clone 253746 3'. 533 e-149 D59844, HUM070E11A Human fetal brain cDNA 3'-end GEN-070E11. 466 e-129 H11525, H11525 ym15h07.s1 Homo sapiens cDNA clone 48232 3'. 442 e-122 AA971254, AA971254 op73c08.s1 Soares\_NFL T\_GBC\_S1 Homo sapien... 442 e-122 W77907, W77907 zd70f08.rl Soares fetal heart NbHH19W Homo sap... 428 e-118 AA878973, AA878973 oj26d11.s1 NCI\_CGAP\_Kid3 Homo sapiens cDNA... 389 e-106 AA715235, AA715235 nv10g01.s1 NCI\_CGAP Pr22 Homo sapiens cDNA... 357 2e-96

AA328928, AA328928 EST32475 Embryo, 12 week I Homo sapiens cD... 355 7e-96 AA860455, AA860455 aj80f02.s1 Soares parathyroid tumor NbHPA ... 283 2e-74 AA026096, AA026096 ze97a04.rl Soares fetal heart NbHH19W Homo... 268 le-69 AA026516, AA026516 ze97a04.s1 Soares fetal heart NbHH19W Homo... 172 6e-41 T26899, T26899 ESTDIR509 Homo sapiens cDNA clone CDDIR509 3'. 170 2e-40 N71178, N71178 yw30c10.rl Homo sapiens cDNA clone 253746 5'. 165 1e-38 AA372290, AA372290 EST84170 Raji cells, cyclohexamide treated... 98 3e-18 AI038890, AI038890 ox84g12.x1 Soares senescent fibroblasts Nb... D81647, HUM180D08B Human fetal brain cDNA 5'-end GEN-180D08. 38 2.1 AA452630, AA452630 zx33f08.rl Soares total fetus Nb2HF8 9w Ho... 38 2.1 AA682624, AA682624 zi19g01.s1 Soares fetal liver spleen 1NFLS... 38 2.1 AA742364, AA742364 ny89c12.s1 NCI\_CGAP GCB1 Homo sapiens cDNA... 38 2.1 AA907234, AA907234 ol03h08.s1 NCI\_CGAP\_Lu5 Homo sapiens cDNA ... 38 2.1 T09391, T09391 EST07284 Homo sapiens cDNA clone HIBBT71 5' en... 38 2.1 AA161236, AA161236 zo59h07.s1 Stratagene pancreas (#937208) H... 38 2.1 AA252941, AA252941 zr50g09.rl Soares NhHMPu S1 Homo sapiens c... 38 2.1 AA252245, AA252245 zr64g07.s1 Soares NhHMPu S1 Homo sapiens c... AA780678, AA780678 ac70h01.s1 Stratagene fetal retina 937202 ... 38 2.1 W05501, W05501 za84a12.rl Soares fetal lung NbHL19W Homo sapi... 38 2.1 AI039908, AI039908 ox25f07.x1 Soares\_total\_fetus\_Nb2HF8 9w Ho... 38 2.1 AA280664, AA280664 zs99f09.s1 NCI\_CGAP GCB1 Homo sapiens cDNA... 38 2.1 AA973566, AA973566 oo46f09.s1 NCI\_CGAP\_Lu5 Homo sapiens cDNA ... 38 2.1 N27253, N27253 yx17g01.rl Homo sapiens cDNA clone 262032 5'. AA995707, AA995707 os29c09.s1 NCI\_CGAP\_Kid5 Homo sapiens cDNA... 38 2.1 AI016407, AI016407 ot72e09.s1 Soares\_total\_fetus Nb2HF8\_9w Ho... 38 2.1 N70619, N70619 za84a12.s1 Homo sapiens cDNA clone 299230 3'. AA242923, AA242923 zr64g07.r1 Soares NhHMPu S1 Homo sapiens c... 38 2.1 AA938631, AA938631 0096f07.s1 NCI\_CGAP Kid5 Homo sapiens cDNA... 38 2.1 AA985290, AA985290 am74g03.s1 Stratagene schizo brain S11 Hom... 38 2.1

AA690806, AA690806 vt25h10.rl Barstead mouse myotubes MPLRB5 ... 377 e-103 AA155014, AA155014 mr99h05.rl Stratagene mouse embryonic carc... 180 8e-44 AA269966, AA269966 va57d06.rl Soares mouse 3NME12 5 Mus muscu... 172 2e-41 AA089195, AA089195 mo05h11.rl Stratagene mouse lung 937302 Mu... 163 2e-38 AA466212, AA466212 vg86g02.rl Barstead mouse pooled organs MP... 68 8e-10 AA423476, AA423476 ve76d07.rl Soares mouse mammary gland NbMM... 60 2e-07 AA597213, AA597213 vo28a05.rl Barstead mouse irradiated colon... 40 0.19 AA396266, AA396266 vb45c01.rl Soares mouse lymph node NbMLN M... 40 0.19 AA967806, AA967806 uh05d06.rl Soares mouse hypothalamus NMHy ... 38 0.75 AA591111, AA591111 vm12c06.rl Knowles Solter mouse blastocyst... 38 0.75 W65797, W65797 me14g02.rl Soares mouse embryo NbME13.5 14.5 M... 38 0.75 AA153891, AA153891 mq56e05.rl Soares 2NbMT Mus musculus cDNA ... 38 0.75

AI019772, AI019772 ua90h02.rl Soares mouse mammary gland NbMM 36 3.0
AA472253, AA472253 vh10g05.rl Soares mouse mammary gland NbMM 36 3.0
AA230895, AA230895 mw14g07.r1 Soares mouse 3NME12 5 Mus muscu 36 3.0
W18052, W18052 mb83g03.r1 Soares mouse p3NMF19.5 Mus musculus 36 3.0
AA797681, AA797681 vx66c12.rl Stratagene mouse skin (#937313) 36 3.0
W66734, W66734 me26g05.r1 Soares mouse embryo NbME13.5 14.5 M 36 3.0
AA968020, AA968020 uh07g01.rl Soares mouse hypothalamus NMHy 36 3.0
A A O F 1 C A A A O F 1 C A A A C F 1 A C A C A C A C A C A C A C A C A C A
A A 1 COTOTA A A 1 COTOTA DO DO 1 C
AA162/9/, AA162/9/ mr29g09.r1 Soares mouse 3NbMS Mus musculus 36 3.0
AA549644, AA549644 vk80f08.s1 Knowles Solter mouse 2 cell Mus 36 3.0
AA273295, AA273295 vc01e01.rl Soares mouse lymph node NbMLN M 36 3.0
AA048480, AA048480 mj33d08.rl Soares mouse embryo NbME13.5 14 36 3.0
AA098207, AA098207 mn83d01.r1 Stratagene mouse Tcell 937311 M 36 3.0
AA027381, AA027381 mi05c06.rl Soares mouse placenta 4NbMP13.5 36 3.0
AA544474, AA544474 vk33h06.rl Soares mouse mammary gland NbMM 36 3.0
AA416466, AA416466 vd15c09.s1 Knowles Solter mouse 2 cell Mus 36 3.0
AA285999, AA285999 vb88h08.rl Soares mouse 3NbMS Mus musculus 36 3.0
AA175025, AA175025 ms85f06.rl Soares mouse 3NbMS Mus musculus 36 3.0
AA544386, AA544386 vk33f06.r1 Soares mouse mammary gland NbMM 36 3.0
AA175557, AA175557 ms96g04.r1 Soares mouse 3NbMS Mus musculus 36 3.0
AA711924, AA711924 vu59f09.rl Soares mouse mammary gland NbMM 36 3.0
AA734052, AA734052 vv22c10.r1 Stratagene mouse heart (#937316 36 3.0
W. 62 72 0 W. 62 72 0 1 0 1 0 1 0 1 0 1 0 1 0 1 0 1 0 1 0
W53/38, W53/38 md12a12.r1 Soares mouse embryo NbME13.5 14.5 M 36 3.0
AA611837, AA611837 vo82a06.r1 Barstead mouse myotubes MPLRB5 36 3.0
AA879531, AA879531 vv96f06.rl Soares mouse mammary gland NbMM 36 3.0
AA288625, AA288625 vb23g09.r1 Soares mouse 3NbMS Mus musculus 36 3.0

AA784124, AA784124 d2b06a1.fl Aspergillus nidulans 24hr asexu... 38 0.67 AI044911, AI044911 UI-R-C1-kk-e-05-0-UI.sl UI-R-C1 Rattus nor... 36 2.6 AA550452, AA550452 1605m3 gmbPfHB3.1, G. Roman Reddy Plasmodi... 36 2.6 F20017, ATTS6056 A. thaliana transcribed sequence; clone TAP... 36 2.6 AA786697, AA786697 k5d01a1.fl Aspergillus nidulans 24hr asexu... 36 2.6 AA433457, AA433457 SW3ICA2345SK Brugia malayi infective larva... 36 2.6

SEQ ID NO:550

U66201, MMU66201 Mus musculus fibroblast growth factor homolo... 42 0.20 AF020738, AF020738 Mus musculus fibroblast growth factor-rela... 42 0.20 U66197, HSU66197 Human fibroblast growth factor homologous fa... 42 0.20 Z46966, MMIMOGN44 M.musculus mRNA for imogen 44. 40 0.80

AC004301, AC004301 Drosophila melanogaster DNA sequence (P1 D... 40 0.80 U86662, LEU86662 Lycopersicon esculentum VPS41 (tVPS41) mRNA,... 40 0.80 Y14330, HSY14330 Homo sapiens partial mRNA for jagged2 protein AF003521, AF003521 Homo sapiens Jagged 2 mRNA, complete cds AF029778, AF029778 Homo sapiens Jagged2 (JAG2) mRNA, complete... 38 3.2 AF020201, AF020201 Homo sapiens Jagged 2 mRNA, complete cds 38 3.2 Z71523, SCYNL247W S.cerevisiae chromosome XIV reading frame ... 38 3.2 AF029779, AF029779 Homo sapiens hJAG2.del-E6 (JAG2) mRNA, alt... 38 3.2 U70049, RNU70049 Rattus norvegicus jagged2 precursor gene, pa... 38 3.2 X96722, SCCHXIVL S.cerevisiae DNA region from chromosome XIV... 38 3.2 AF005938, AF005938 Cavia porcellus L-type voltage-dependent c... 38 3.2 X78972, SBSTRBF S.bluensis ISP 5564 genes strB and strF 38 3.2 X94912, HSPR22 H.sapiens Pr22 gene 38 3.2

# **HUMAN ESTs**

AA860926, AA860926 ak22d06.s1 Soares testis NHT Homo sapiens ... 650 0.0 AA348243, AA348243 EST54707 Hippocampus I Homo sapiens cDNA 5... 513 e-144 AA551799, AA551799 nk04a11.s1 NCI\_CGAP\_Co2 Homo sapiens cDNA ... 363 2e-98 AA327309, AA327309 EST30621 Colon I Homo sapiens cDNA 5' end 353 2e-95 AA344913, AA344913 EST50856 Gall bladder II Homo sapiens cDNA... 337 1e-90 AA121174, AA121174 zl88g08.s1 Stratagene colon (#937204) Homo... 317 le-84 AA121198, AA121198 zl88g08.rl Stratagene colon (#937204) Homo... 317 le-84 AA001561, AA001561 ze46e07.s1 Soares retina N2b4HR Homo sapie... 42 0.098 AI005204, AI005204 ou60c12.x1 NCI\_CGAP\_Br2 Homo sapiens cDNA ... 40 0.39 AA757360, AA757360 ah98a01.s1 Soares NFL T GBC S1 Homo sapien... 40 0.39 AI005324, AI005324 ou13h07.x1 Soares NFL T GBC S1 Homo sapien... 40 0.39 AA416559, AA416559 zu18c03.rl Soares NhHMPu S1 Homo sapiens c... 40 0.39 AA262162, AA262162 zs25b12.rl NCI\_CGAP\_GCB1 Homo sapiens cDNA... AA824270, AA824270 aj29f01.s1 Soares testis NHT Homo sapiens ... 40 0.39 AA826741, AA826741 85f12.s1 NCI\_CGAP\_Pr24 Homo sapiens cDNA... 40 0.39 AA813115, AA813115 aj44d06.s1 Soares testis NHT Homo sapiens ... 40 0.39 AA403143, AA403143 zv66d01.rl Soares total fetus Nb2HF8 9w Ho... 40 0.39 AA725024, AA725024 ah97h10.s1 Soares NFL T GBC S1 Homo sapien... 40 0.39 AA804907, AA804907 oa89a01.s1 NCI\_CGAP\_GCB1 Homo sapiens cDNA... 40 0.39 AA628544, AA628544 af27h12.s1 Soares total fetus Nb2HF8 9w Ho... 40 0.39 AA618498, AA618498 np30a11.s1 NCI CGAP Pr22 Homo sapiens cDNA... 40 0.39 AA503727, AA503727 ne49g02.s1 NCI\_CGAP\_Co3 Homo sapiens cDNA ... 40 0.39 AA460961, AA460961 zx63b07.s1 Soares total fetus Nb2HF8 9w Ho... 40 0.39 AA770473, AA770473 ah89h06.s1 Soares NFL T GBC S1 Homo sapien... 40 0.39 AA759377, AA759377 ah54a10.s1 Soares testis NHT Homo sapiens ... 40 0.39 AA629243, AA629243 zu77e03.s1 Soares testis NHT Homo sapiens ... 40 0.39 AA903406, AA903406 ok62c11.s1 NCI CGAP GC4 Homo sapiens cDNA ... 40 0.39 AA215903, AA215903 hp0042.seq.F Fetal heart, Lambda ZAP Expre... 40 0.39

AA160827, AA160827 zo62e01.s1 Stratagene pancreas (#937208) H... 40 0.39 AA577174, AA577174 nm86e11.s1 NCI CGAP Co9 Homo sapiens cDNA ... 40 0.39 AA969632, AA969632 op38h05.s1 Soares NFL T GBC S1 Homo sapien... 40 0.39 N72025, N72025 yz96g02.s1 Homo sapiens cDNA clone 290930 3'. AA974988, AA974988 on59b06.s1 Soares NFL T GBC S1 Homo sapien... 40 0.39 W32428, W32428 zc05c12.s1 Soares parathyroid tumor NbHPA Homo... 40 0.39 N21678, N21678 yx63g01.s1 Soares melanocyte 2NbHM Homo sapien... 40 0.39 AA860208, AA860208 ak48c10.s1 Soares testis NHT Homo sapiens ... 40 0.39 AA814296, AA814296 nz07d08.s1 NCI\_CGAP\_GCB1 Homo sapiens cDNA... 40 0.39 AA806381, AA806381 oc22g05.s1 NCI CGAP GCB1 Homo sapiens cDNA... 40 0.39 AA435587, AA435587 zt85d07.s1 Soares testis NHT Homo sapiens ... 40 0.39 W45005, W45005 zc05c12.rl Soares parathyroid tumor NbHPA Homo... 40 0.39 AA393904, AA393904 zt85e06.rl Soares testis NHT Homo sapiens ... 40 0.39 AA759038, AA759038 ah75h11.s1 Soares testis NHT Homo sapiens ... 40 0.39 AA927863, AA927863 om18a08.s1 Soares\_NFL\_T\_GBC\_S1 Homo sapien... 40 0.39 AA461270, AA461270 zx63b07.rl Soares total fetus Nb2HF8 9w Ho... 40 0.39 AA417295, AA417295 zu18c03.s1 Soares NhHMPu S1 Homo sapiens c... 40 0.39 W47466, W47466 zc34h02.rl Soares senescent fibroblasts NbHSF ... 40 0.39 AA262229, AA262229 zs25b12.s1 NCI\_CGAP\_GCB1 Homo sapiens cDNA... 40 0.39 AA587486, AA587486 nn84e09.s1 NCI\_CGAP Br2 Homo sapiens cDNA ... 40 0.39 AA401079, AA401079 zv66d01.s1 Soares total fetus Nb2HF8 9w Ho... 40 0.39 AA872272, AA872272 oh72a11.s1 NCI CGAP Kid5 Homo sapiens cDNA... 40 0.39 W47341, W47341 zc34h02.s1 Soares senescent fibroblasts NbHSF ... 40 0.39 N72024, N72024 yz96g01.s1 Homo sapiens cDNA clone 290928 3'. 40 0.39 N35076, N35076 yy19b08.s1 Homo sapiens cDNA clone 271671 3'. 40 0.39 AI040354, AI040354 oy33d12.x1 Soares parathyroid tumor NbHPA ... 40 0.39 AA946650, AA946650 oq38h09.s1 NCI\_CGAP Kid5 Homo sapiens cDNA... 40 0.39 AA022495, AA022495 ze70e04.s1 Soares fetal heart NbHH19W Homo... 40 0.39 AA873216, AA873216 oh70f04.s1 NCI CGAP Kid5 Homo sapiens cDNA... 40 0.39 R82551, R82551 yj19d06.rl Homo sapiens cDNA clone 149195 5'. 38 1.5 H30248, H30248 yp42a01.s1 Homo sapiens cDNA clone 190056 3'. AA161105, AA161105 zo58c05.s1 Stratagene pancreas (#937208) H... 38 1.5 AA948291, AA948291 oq34d02.s1 NCI CGAP GC4 Homo sapiens cDNA ... 38 1.5 AA416734, AA416734 zu08c01.s1 Soares testis NHT Homo sapiens ... 38 1.5 AA431486, AA431486 zw72g01.s1 Soares testis NHT Homo sapiens ... 38 1.5 AA416815, AA416815 zu08c01.rl Soares testis NHT Homo sapiens ... 38 1.5

AA616807, AA616807 vn68c05.r1 Barstead mouse irradiated colon... 180 6e-44
AA467482, AA467482 ve01a10.r1 Soares mouse NbMH Mus musculus ... 40 0.14
AA543280, AA543280 vj80h05.r1 Soares mouse mammary gland NbMM... 40 0.14
AA009071, AA009071 mg87b11.r1 Soares mouse embryo NbME13.5 14... 40 0.14
AA106439, AA106439 ml59a08.r1 Stratagene mouse testis (#93730... 40 0.14

AA014768, AA014768 mi66h04.rl Soares mouse embryo NbME13.5 14... 40 0.14 AA881111, AA881111 vz06e09.r1 Soares mouse mammary gland NbMM... 40 0.14 AA049011, AA049011 mj48c09.rl Soares mouse embryo NbME13.5 14... 40 0.14 AA185487, AA185487 mt62c07.r1 Soares 2NbMT Mus musculus cDNA ... 40 0.14 AA763419, AA763419 vw54a12.rl Soares mouse mammary gland NMLM... 40 0.14 AA016868, AA016868 mh36e12.rl Soares mouse placenta 4NbMP13.5... 40 0.14 AA833479, AA833479 uc91c03.r1 Soares mouse uterus NMPu Mus mu... 40 0.14 AA790448, AA790448 vw04f09.r1 Soares mouse mammary gland NbMM... 40 0.14 AA711859, AA711859 vu59c10.rl Soares mouse mammary gland NbMM... 40 0.14 AA469884, AA469884 vf71g10.r1 Barstead mouse pooled organs MP... 40 0.14 AA230758, AA230758 my32g10.rl Barstead mouse pooled organs MP... 40 0.14 AA497479, AA497479 vh29b12.r1 Soares mouse mammary gland NbMM... 40 0.14 AA138067, AA138067 mq37c11.rl Barstead MPLRB1 Mus musculus cD... 40 0.14 AA103139, AA103139 mo17f05.rl Life Tech mouse embryo 13 5dpc ... 40 0.14 AI047077, AI047077 uh61g06.rl Soares mouse embryonic stem cel... 40 0.14 AI048515, AI048515 uh61e08.rl Soares mouse embryonic stem cel... 40 0.14 W61547, W61547 md57a02.r1 Soares mouse embryo NbME13.5 14.5 M... 40 0.14 AA007762, AA007762 mg76b03.rl Soares mouse embryo NbME13.5 14... 40 0.14 AA000268, AA000268 mg32e09.rl Soares mouse embryo NbME13.5 14... 40 0.14 AA475425, AA475425 vh20g09.rl Soares mouse mammary gland NbMM... AA014223, AA014223 mh20a03.rl Soares mouse placenta 4NbMP13.5... 40 0.14 AA797372, AA797372 vw27b08.r1 Soares mouse mammary gland NbMM... 40 0.14 AA106301, AA106301 ml81a09.rl Stratagene mouse kidney (#93731... 40 0.14 AA033481, AA033481 mi42b07.rl Soares mouse embryo NbME13.5 14... 40 0.14 W77724, W77724 me84h06.r1 Soares mouse embryo NbME13.5 14.5 M... 40 0.14 W83172, W83172 mf09a06.rl Soares mouse p3NMF19.5 Mus musculus... 40 0.14 AA038869, AA038869 mi95b10.rl Soares mouse p3NMF19.5 Mus musc... 40 0.14 AA068686, AA068686 mm59a03.rl Stratagene mouse embryonic carc... 38 0.55 AA111190, AA111190 mp66b11.rl Soares 2NbMT Mus musculus cDNA ... 36 2.2 AA840087, AA840087 uc99h12.r1 Soares mouse uterus NMPu Mus mu... 36 2.2 AA239210, AA239210 mx89e02.rl Soares mouse NML Mus musculus c... 36 2.2 AA824205, AA824205 vy20g08.r1 Stratagene mouse macrophage (#9... 36 2.2 C87249, C87249 Mus musculus fertilized egg cDNA 3'-end seque... 36 2.2 AA089210, AA089210 mo05d10.r1 Stratagene mouse lung 937302 Mu... 36 2.2 AA711873, AA711873 vu28e06.r1 Barstead mouse myotubes MPLRB5 ... 36 2.2 AA793845, AA793845 vr35e12.rl Barstead mouse myotubes MPLRB5 ... 36 2.2 AA645119, AA645119 vs72d03.r1 Stratagene mouse skin (#937313)... 36 2.2 AA967316, AA967316 vj47a03.rl Stratagene mouse skin (#937313)... 36 2.2 W87202, W87202 mf55g08.r1 Soares mouse embryo NbME13.5 14.5 M... 36 2.2 AA218431, AA218431 my07e05.rl Barstead mouse lung MPLRB2 Mus ... 36 2.2 AA796056, AA796056 vo65d01.rl Soares mouse mammary gland NbMM... 36 2.2 AA542324, AA542324 vk53e07.r1 Stratagene mouse Tcell 937311 M... 36 2.2 AA530735, AA530735 vj32g11.r1 Stratagene mouse diaphragm (#93... 36 2.2 AI047609, AI047609 uh63g07.rl Soares mouse embryonic stem cel... 36 2.2 AA591243, AA591243 vm18c04.r1 Knowles Solter mouse blastocyst... 36 2.2

AA856298, AA856298 vw99b01.r1 Soares 2NbMT Mus musculus cDNA ... 36 2.2 AA966976, AA966976 ua38f11.r1 Soares mouse mammary gland NbMM... 36 2.2

AA957268, AA957268 UI-R-E1-fq-e-06-0-UI.s1 UI-R-E1 Rattus nor... 42 0.031 AA801145, AA801145 EST190642 Normalized rat ovary, Bento Soar... AI012760, AI012760 EST207211 Normalized rat placenta, Bento S... 38 0.48 AA874930, AA874930 UI-R-E0-ci-b-05-0-UI.s1 UI-R-E0 Rattus nor... C82607, C82607 Oryctolagus cuniculus corneal endothelial cDN... 38 0.48 AA859865, AA859865 UI-R-E0-cc-b-04-0-UI.s1 UI-R-E0 Rattus nor... 38 0.48 C83463, C83463 Oryctolagus cuniculus corneal endothelial cDN... 38 0.48 AA801144, AA801144 EST190641 Normalized rat ovary, Bento Soar... AA859448, AA859448 UI-R-A0-bf-b-01-0-UI.s1 UI-R-A0 Rattus nor... AI009631, AI009631 EST204082 Normalized rat lung, Bento Soare... 38 0.48 AI009035, AI009035 EST203486 Normalized rat embryo, Bento Soa... 38 0.48 AA859542, AA859542 UI-R-E0-br-d-03-0-UI.s1 UI-R-E0 Rattus nor... H32878, H32878 EST108396 Rat PC-12 cells, untreated Rattus sp... 36 1.9 AA943364, AA943364 EST198863 Normalized rat brain, Bento Soar... 36 1.9 Z32602, ATTS2730 A. thaliana transcribed sequence; clone PAP... 36 1.9 Z33974, ATTS3035 A. thaliana transcribed sequence; clone PAP... 36 1.9 Z32603, ATTS2731 A. thaliana transcribed sequence; clone PAP... 36 1.9 AA660859, AA660859 00754 MtRHE Medicago truncatula cDNA 5' si... 36 1.9 AA842765, AA842765 M-EST080 Sugarcane mature stalk Saccharum ... 36 1.9 AA125602, AA125602 JM00M011.QM3 Miracidia Sjc 3/96 Schistosom... 36 1.9 AA785775, AA785775 h4b05a1.fl Aspergillus nidulans 24hr asexu... 36 1.9

#### **SEQ ID NO:551**

U66201, MMU66201 Mus musculus fibroblast growth factor homolo... 42 0.36 AF020738, AF020738 Mus musculus fibroblast growth factor-rela... 42 0.36 U66197, HSU66197 Human fibroblast growth factor homologous fa... 42 0.36 U86662, LEU86662 Lycopersicon esculentum VPS41 (tVPS41) mRNA,... 40 1.4 U85773, HSU85773 Human phosphomannomutase (PMM2) mRNA, comple... 40 1.4 Z46966, MMIMOGN44 M.musculus mRNA for imogen 44. 40 1.4 AC004301, AC004301 Drosophila melanogaster DNA sequence (P1 D... 40 1.4

# **HUMAN ESTs**

W22160, W22160 63A6 Human retina cDNA Tsp509I-cleaved sublibr... 791 0.0 AA860926, AA860926 ak22d06.s1 Soares testis NHT Homo sapiens ... 650 0.0

AA348243, AA348243 EST54707 Hippocampus I Homo sapiens cDNA 5... 513 e-143 AA551799, AA551799 nk04a11.s1 NCI CGAP Co2 Homo sapiens cDNA ... 363 4e-98 AA327309, AA327309 EST30621 Colon I Homo sapiens cDNA 5' end 353 4e-95 AA344913, AA344913 EST50856 Gall bladder II Homo sapiens cDNA... 337 2e-90 AA121174, AA121174 zl88g08.s1 Stratagene colon (#937204) Homo... 317 2e-84 AA121198, AA121198 zl88g08.r1 Stratagene colon (#937204) Homo... 317 2e-84 AA001561, AA001561 ze46e07.s1 Soares retina N2b4HR Homo sapie... 42 0.17 AA877455, AA877455 ob33g01.s1 NCI\_CGAP\_Kid5 Homo sapiens cDNA... 40 0.68 N35888, N35888 yy28b05.s1 Homo sapiens cDNA clone 272529 3'. AA040802, AA040802 zf07g05.s1 Soares fetal heart NbHH19W Homo... 40 0.68 AA573297, AA573297 nk98d09.s1 NCI\_CGAP\_Co3 Homo sapiens cDNA ... 40 0.68 AA041240, AA041240 zf07g05.rl Soares fetal heart NbHH19W Homo... 40 0.68 AA514777, AA514777 ni24b01.sl NCI CGAP Co4 Homo sapiens cDNA ... 40 0.68 R02514, R02514 ye70b08.rl Homo sapiens cDNA clone 123063 5'. 40 0.68 AA039536, AA039536 zk39h10.s1 Soares pregnant uterus NbHPU Ho... 40 0.68 AA888147, AA888147 04h11.s1 NCI CGAP Co10 Homo sapiens cDNA... 40 0.68 AA172158, AA172158 zp29a01.s1 Stratagene neuroepithelium (#93... 40 0.68 AA416734, AA416734 zu08c01.s1 Soares testis NHT Homo sapiens ... 38 2.7 N98472, N98472 yy65a04.rl Homo sapiens cDNA clone 278382 5'. 38 2.7 AA416815, AA416815 zu08c01.rl Soares testis NHT Homo sapiens ... 38 2.7 AA852281, AA852281 NHTBCae11g05r1 Normal Human Trabecular Bon... 38 2.7 AA948291, AA948291 oq34d02.s1 NCI CGAP GC4 Homo sapiens cDNA ... 38 2.7 R14449, R14449 yf81h09.r1 Homo sapiens cDNA clone 29034 5'. AA431486, AA431486 zw72g01.s1 Soares testis NHT Homo sapiens ... 38 2.7

AA616807, AA616807 vn68c05.rl Barstead mouse irradiated colon... 180 1e-43 AA469884, AA469884 vf71g10.rl Barstead mouse pooled organs MP... 40 0.24 AA038869, AA038869 mi95b10.rl Soares mouse p3NMF19.5 Mus musc... 40 0.24 AA185487, AA185487 mt62c07.r1 Soares 2NbMT Mus musculus cDNA ... AA230758, AA230758 my32g10.rl Barstead mouse pooled organs MP... 40 0.24 AA276740, AA276740 vc42a12.rl Soares mouse 3NbMS Mus musculus... 40 0.24 AA763419, AA763419 vw54a12.rl Soares mouse mammary gland NMLM... 40 0.24 AA106439, AA106439 ml59a08.rl Stratagene mouse testis (#93730... 40 0.24 AA250010, AA250010 mz59b12.rl Soares mouse lymph node NbMLN M... 38 0.97 AA068686, AA068686 mm59a03.r1 Stratagene mouse embryonic carc... 38 0.97 AA139459, AA139459 mq86a03.r1 Stratagene mouse melanoma (#937... 38 0.97 AA881111, AA881111 vz06e09.rl Soares mouse mammary gland NbMM... 36 3.8 AA692425, AA692425 vt59b05.rl Barstead mouse irradiated colon... 36 3.8 AA049011, AA049011 mj48c09.rl Soares mouse embryo NbME13.5 14... 36 3.8 AA966976, AA966976 ua38f11.r1 Soares mouse mammary gland NbMM... 36 3.8 AI047077, AI047077 uh61g06.rl Soares mouse embryonic stem cel... 36 3.8 AA103139, AA103139 mo17f05.rl Life Tech mouse embryo 13 5dpc ... 36 3.8

AA840087, AA840087 uc99h12.rl Soares mouse uterus NMPu Mus mu 36 3.8
AA543280, AA543280 vj80h05.rl Soares mouse mammary gland NbMM 36 3.8
AA007762, AA007762 mg76b03.rl Soares mouse embryo NbME13.5 14 36 3.8
AA014223, AA014223 mh20a03.rl Soares mouse placenta 4NbMP13.5 36 3.8
AA591243, AA591243 vm18c04.rl Knowles Solter mouse blastocyst 36 3.8
AA921560, AA921560 vy52c06.rl Stratagene mouse lung 937302 Mu 36 3.8
W20935, W20935 mb96c07.rl Soares mouse p3NMF19.5 Mus musculus 36 3.8
AA793845, AA793845 vr35e12.rl Barstead mouse myotubes MPLRB5 36 3.8
AA856298, AA856298 vw99b01.rl Soares 2NbMT Mus musculus cDNA 36 3.8
AA833479, AA833479 uc91c03.rl Soares mouse uterus NMPu Mus mu 36 3.8
AA218431, AA218431 my07e05.rl Barstead mouse lung MPLRB2 Mus 36 3.8
AA089210, AA089210 mo05d10.r1 Stratagene mouse lung 937302 Mu 36 3.8
AI047609, AI047609 uh63g07.rl Soares mouse embryonic stem cel 36 3.8
AA797372, AA797372 vw27b08.rl Soares mouse mammary gland NbMM 36 3.8
AA138067, AA138067 mq37c11.rl Barstead MPLRB1 Mus musculus cD 36 3.8
W83172, W83172 mf09a06.rl Soares mouse p3NMF19.5 Mus musculus 36 3.8
AA542324, AA542324 vk53e07.rl Stratagene mouse Tcell 937311 M 36 3.8
AA967316, AA967316 vj47a03.r1 Stratagene mouse skin (#937313) 36 3.8
AI035925, AI035925 ub49e05.rl Soares mouse mammary gland NbMM 36 3.8
AA497479, AA497479 vh29b12.rl Soares mouse mammary gland NbMM 36 3.8
W87202, W87202 mf55g08.r1 Soares mouse embryo NbME13.5 14.5 M 36 3.8
AA016868, AA016868 mh36e12.r1 Soares mouse placenta 4NbMP13.5 36 3.8
AA467482, AA467482 ve01a10.r1 Soares mouse NbMH Mus musculus 36 3.8
AA014768, AA014768 mi66h04.rl Soares mouse embryo NbME13.5 14 36 3.8
AA711859, AA711859 vu59c10.rl Soares mouse mammary gland NbMM 36 3.8
AA530735, AA530735 vj32g11.rl Stratagene mouse diaphragm (#93 36 3.8
AA009071, AA009071 mg87b11.r1 Soares mouse embryo NbME13.5 14 36 3.8
AA711873, AA711873 vu28e06.rl Barstead mouse myotubes MPLRB5 36 3.8
AA645119, AA645119 vs72d03.rl Stratagene mouse skin (#937313) 36 3.8
AA106301, AA106301 ml81a09.rl Stratagene mouse kidney (#93731 36 3.8
AA111190, AA111190 mp66b11.rl Soares 2NbMT Mus musculus cDNA 36 3.8
C87249, C87249 Mus musculus fertilized egg cDNA 3'-end seque 36 3.8
AA796056, AA796056 vo65d01.rl Soares mouse mammary gland NbMM 36 3.8
AA230661, AA230661 mw15f08.rl Soares mouse 3NME12 5 Mus muscu 36 3.8
AA033481, AA033481 mi42b07.r1 Soares mouse embryo NbME13.5 14 36 3.8
AA000268, AA000268 mg32e09.rl Soares mouse embryo NbME13.5 14 36 3.8
AI048515, AI048515 uh61e08.rl Soares mouse embryonic stem cel 36 3.8
W61547, W61547 md57a02.r1 Soares mouse embryo NbME13.5 14.5 M 36 3.8
AA790448, AA790448 vw04f09.rl Soares mouse mammary gland NbMM 36 3.8
AA824205, AA824205 vy20g08.r1 Stratagene mouse macrophage (#9 36 3.8
AA475425, AA475425 vh20g09.rl Soares mouse mammary gland NbMM 36 3.8
W62989, W62989 md88h12.r1 Soares mouse embryo NbME13.5 14.5 M 36 3.8
W77724, W77724 me84h06.r1 Soares mouse embryo NbME13.5 14.5 M 36 3.8
AA239210, AA239210 mx89e02.rl Soares mouse NML Mus musculus c 36 3.8
11 1237216, 11 1237216 Introversit Source invase that interest the interest to 3.6

AA957268, AA957268 UI-R-E1-fq-e-06-0-UI.s1 UI-R-E1 Rattus nor... 42 0.055 AA891284, AA891284 EST195087 Normalized rat heart, Bento Soar... 40 0.22 Z83055, RNZ83055 R.norvegicus mRNA; expressed sequence tag; ... 40 0.22 AI010967, AI010967 EST205418 Normalized rat muscle, Bento Soa... 40 0.22 AA852049, AA852049 EST194818 Normalized rat spleen, Bento Soa... 40 0.22 H33489, H33489 EST109542 Rat PC-12 cells, NGF-treated (9 days... 40 0.22 AA799616, AA799616 EST189113 Normalized rat heart, Bento Soar... 40 0.22 Z83044, RNZ83044 R.norvegicus mRNA; expressed sequence tag; ... 40 0.22 AA660819, AA660819 00713 MtRHE Medicago truncatula cDNA 5' 38 0.86 AA956139, AA956139 UI-R-E1-fi-h-08-0-UI.s1 UI-R-E1 Rattus nor... 38 0.86 T00613, T00613 wEST01334 Caenorhabditis elegans cDNA clone CE... 38 0.86 AA785775, AA785775 h4b05a1.fl Aspergillus nidulans 24hr asexu... 36 3.4 AA660859, AA660859 00754 MtRHE Medicago truncatula cDNA 5' si... 36 3.4 AA943364, AA943364 EST198863 Normalized rat brain, Bento Soar... 36 3.4 C68472, C68472 C.elegans cDNA clone yk305a12: 5' end, singl... 36 3.4 AA800635, AA800635 EST190132 Normalized rat lung, Bento Soare... Z32602, ATTS2730 A. thaliana transcribed sequence; clone PAP... 36 3.4 Z32603, ATTS2731 A. thaliana transcribed sequence; clone PAP... AA842765, AA842765 M-EST080 Sugarcane mature stalk Saccharum ... 36 3.4 AA955567, AA955567 UI-R-E1-fa-a-08-0-UI.s1 UI-R-E1 Rattus nor... 36 3.4 H32878, H32878 EST108396 Rat PC-12 cells, untreated Rattus sp... 36 3.4 Z33974, ATTS3035 A. thaliana transcribed sequence; clone PAP... 36 3.4 D45997, RICS10346A Rice cDNA, partial sequence (S10346 1A). 36 3.4 AA125602, AA125602 JM00M011.QM3 Miracidia Sjc 3/96 Schistosom... 36 3.4 AA800634, AA800634 EST190131 Normalized rat lung, Bento Soare... 36 3.4 D46069, RICS10475A Rice cDNA, partial sequence (S10475 1A).

# SEQ ID NO:552

U66201, MMU66201 Mus musculus fibroblast growth factor homolo... 42 0.38
AF020738, AF020738 Mus musculus fibroblast growth factor-rela... 42 0.38
U66197, HSU66197 Human fibroblast growth factor homologous fa... 42 0.38
Z46966, MMIMOGN44 M.musculus mRNA for imogen 44. 40 1.5
U86662, LEU86662 Lycopersicon esculentum VPS41 (tVPS41) mRNA,... 40 1.5
U85773, HSU85773 Human phosphomannomutase (PMM2) mRNA, comple... 40 1.5

# **HUMAN ESTs**

W22160, W22160 63A6 Human retina cDNA Tsp509I-cleaved sublibr... 791 0.0 AA860926, AA860926 ak22d06.s1 Soares testis NHT Homo sapiens ... 650 0.0

AA348243, AA348243 EST54707 Hippocampus I Homo sapiens cDNA 5... 513 e-143 AA551799, AA551799 nk04a11.s1 NCI\_CGAP\_Co2 Homo sapiens cDNA ... 363 4e-98 AA327309, AA327309 EST30621 Colon I Homo sapiens cDNA 5' end 353 4e-95 AA344913, AA344913 EST50856 Gall bladder II Homo sapiens cDNA... 337 2e-90 AA121198, AA121198 zl88g08.rl Stratagene colon (#937204) Homo... 317 2e-84 AA121174, AA121174 zl88g08.s1 Stratagene colon (#937204) Homo... 317 2e-84 AA001561, AA001561 ze46e07.s1 Soares retina N2b4HR Homo sapie... 42 0.18 AA172158, AA172158 zp29a01.s1 Stratagene neuroepithelium (#93... 40 0.72 N35888, N35888 yy28b05.s1 Homo sapiens cDNA clone 272529 3'. 40 0.72 AA877455, AA877455 ob33g01.sl NCI\_CGAP\_Kid5 Homo sapiens cDNA... 40 0.72 AA573297, AA573297 nk98d09.s1 NCI CGAP Co3 Homo sapiens cDNA ... 40 0.72 AA040802, AA040802 zf07g05.s1 Soares fetal heart NbHH19W Homo... 40 0.72 R02514, R02514 ye70b08.rl Homo sapiens cDNA clone 123063 5'. AA514777, AA514777 ni24b01.s1 NCI\_CGAP Co4 Homo sapiens cDNA ... 40 0.72 AA041240, AA041240 zf07g05.rl Soares fetal heart NbHH19W Homo... 40 0.72 AA888147, AA888147 04h11.s1 NCI\_CGAP\_Co10 Homo sapiens cDNA... 40 0.72 AA039536, AA039536 zk39h10.s1 Soares pregnant uterus NbHPU Ho... 40 0.72 AA416734, AA416734 zu08c01.s1 Soares testis NHT Homo sapiens ... 38 2.8 N25839, N25839 yx22e05.rl Homo sapiens cDNA clone 262496 5'. 38 2.8 AA431486, AA431486 zw72g01.s1 Soares testis NHT Homo sapiens ... 38 2.8 N98472, N98472 yy65a04.rl Homo sapiens cDNA clone 278382 5'. AA416815, AA416815 zu08c01.rl Soares testis NHT Homo sapiens ... 38 2.8 AA852281, AA852281 NHTBCael1g05rl Normal Human Trabecular Bon... 38 2.8 AA948291, AA948291 oq34d02.s1 NCI\_CGAP\_GC4 Homo sapiens cDNA ... 38 2.8

AA616807, AA616807 vn68c05.rl Barstead mouse irradiated colon... 180 1e-43 AA185487, AA185487 mt62c07.rl Soares 2NbMT Mus musculus cDNA ... 40 0.26 AA276740, AA276740 vc42a12.r1 Soares mouse 3NbMS Mus musculus... 40 0.26 AA469884, AA469884 vf71g10.rl Barstead mouse pooled organs MP... 40 0.26 AA230758, AA230758 my32g10.r1 Barstead mouse pooled organs MP... 40 0.26 AA038869, AA038869 mi95b10.rl Soares mouse p3NMF19.5 Mus musc... 40 0.26 AA106439, AA106439 ml59a08.rl Stratagene mouse testis (#93730... 40 0.26 AA763419, AA763419 vw54a12.rl Soares mouse mammary gland NMLM... 40 0.26 AA139459, AA139459 mq86a03.r1 Stratagene mouse melanoma (#937... 38 1.0 AA068686, AA068686 mm59a03.r1 Stratagene mouse embryonic carc... 38 1.0 AA218431, AA218431 my07e05.rl Barstead mouse lung MPLRB2 Mus ... 36 4.0 AI047077, AI047077 uh61g06.rl Soares mouse embryonic stem cel... 36 4.0 C87249, C87249 Mus musculus fertilized egg cDNA 3'-end seque... 36 4.0 AI035925, AI035925 ub49e05.rl Soares mouse mammary gland NbMM... 36 4.0 AA111190, AA111190 mp66b11.rl Soares 2NbMT Mus musculus cDNA ... 36 4.0 AA645119, AA645119 vs72d03.r1 Stratagene mouse skin (#937313)... 36 4.0 AA530735, AA530735 vj32g11.r1 Stratagene mouse diaphragm (#93... 36 4.0

AA000268, AA000268 mg32e09.rl Soares mouse embryo NbME13.5 14 36 4.0
AA793845, AA793845 vr35e12.r1 Barstead mouse myotubes MPLRB5 36 4.0
AA840087, AA840087 uc99h12.rl Soares mouse uterus NMPu Mus mu 36 4.0
AA711873, AA711873 vu28e06.rl Barstead mouse myotubes MPLRB5 36 4.0
AA790448, AA790448 vw04f09.rl Soares mouse mammary gland NbMM 36 4.0
AA106301, AA106301 ml81a09.rl Stratagene mouse kidney (#93731 36 4.0
AA543280, AA543280 vj80h05.rl Soares mouse mammary gland NbMM 36 4.0
AA007762, AA007762 mg76b03.rl Soares mouse embryo NbME13.5 14 36 4.0
AA921560, AA921560 vy52c06.rl Stratagene mouse lung 937302 Mu 36 4.0
AA692425, AA692425 vt59b05.rl Barstead mouse irradiated colon 36 4.0
AA833479, AA833479 uc91c03.r1 Soares mouse uterus NMPu Mus mu 36 4.0
AA824205, AA824205 vy20g08.rl Stratagene mouse macrophage (#9 36 4.0
AA033481, AA033481 mi42b07.rl Soares mouse embryo NbME13.5 14 36 4.0
W61547, W61547 md57a02.r1 Soares mouse embryo NbME13.5 14.5 M 36 4.0
AA796056, AA796056 vo65d01.rl Soares mouse mammary gland NbMM 36 4.0
AA467482, AA467482 ve01a10.r1 Soares mouse NbMH Mus musculus 36 4.0
AA239210, AA239210 mx89e02.r1 Soares mouse NML Mus musculus c 36 4.0
AA881111, AA881111 vz06e09.rl Soares mouse mammary gland NbMM 36 4.0
AA542324, AA542324 vk53e07.rl Stratagene mouse Tcell 937311 M 36 4.0
AA089210, AA089210 mo05d10.r1 Stratagene mouse lung 937302 Mu 36 4.0
W77724, W77724 me84h06.rl Soares mouse embryo NbME13.5 14.5 M 36 4.0
AI048515, AI048515 uh61e08.r1 Soares mouse embryonic stem cel 36 4.0
AA009071, AA009071 mg87b11.r1 Soares mouse embryo NbME13.5 14 36 4.0
AA475425, AA475425 vh20g09.rl Soares mouse mammary gland NbMM 36 4.0
AA230661, AA230661 mw15f08.r1 Soares mouse 3NME12 5 Mus muscu 36 4.0
AA138067, AA138067 mq37c11.rl Barstead MPLRB1 Mus musculus cD 36 4.0
W83172, W83172 mf09a06.rl Soares mouse p3NMF19.5 Mus musculus 36 4.0
AA797372, AA797372 vw27b08.rl Soares mouse mammary gland NbMM 36 4.0
AA711859, AA711859 vu59c10.rl Soares mouse mammary gland NbMM 36 4.0
AA967316, AA967316 vj47a03.r1 Stratagene mouse skin (#937313) 36 4.0
W87202, W87202 mf55g08.r1 Soares mouse embryo NbME13.5 14.5 M 36 4.0
AA103139, AA103139 mo17f05.rl Life Tech mouse embryo 13 5dpc 36 4.0
AA014223, AA014223 mh20a03.r1 Soares mouse placenta 4NbMP13.5 36 4.0
W62989, W62989 md88h12.r1 Soares mouse embryo NbME13.5 14.5 M 36 4.0
W20935, W20935 mb96c07.r1 Soares mouse p3NMF19.5 Mus musculus 36 4.0
AA966976, AA966976 ua38f11.r1 Soares mouse mammary gland NbMM 36 4.0
AA856298, AA856298 vw99b01.rl Soares 2NbMT Mus musculus cDNA 36 4.0
AA014768, AA014768 mi66h04.rl Soares mouse embryo NbME13.5 14 36 4.0
AA497479, AA497479 vh29b12.rl Soares mouse mammary gland NbMM 36 4.0
AA049011, AA049011 mj48c09.rl Soares mouse embryo NbME13.5 14 36 4.0
AA016868, AA016868 mh36e12.rl Soares mouse placenta 4NbMP13.5 36 4.0
AI047609, AI047609 uh63g07.r1 Soares mouse embryonic stem cel 36 4.0
AA591243, AA591243 vm18c04.r1 Knowles Solter mouse blastocyst 36 4.0

AA957268, AA957268 UI-R-E1-fq-e-06-0-UI.s1 UI-R-E1 Rattus nor... 42 0.058 T00613, T00613 wEST01334 Caenorhabditis elegans cDNA clone CE... 38 0.90 AA956139, AA956139 UI-R-E1-fi-h-08-0-UI.s1 UI-R-E1 Rattus nor... 38 0.90 AA660819, AA660819 00713 MtRHE Medicago truncatula cDNA 5' 38 0.90 AA125602, AA125602 JM00M011.QM3 Miracidia Sjc 3/96 Schistosom... 36 3.6 Z33974, ATTS3035 A. thaliana transcribed sequence; clone PAP... 36 3.6 C68472, C68472 C.elegans cDNA clone yk305a12: 5' end, singl... 36 3.6 AA785775, AA785775 h4b05a1.fl Aspergillus nidulans 24hr asexu... 36 3.6 Z32602, ATTS2730 A. thaliana transcribed sequence; clone PAP... 36 3.6 AA943364, AA943364 EST198863 Normalized rat brain, Bento Soar... 36 3.6 Z32603, ATTS2731 A. thaliana transcribed sequence; clone PAP... 36 3.6 AA842765, AA842765 M-EST080 Sugarcane mature stalk Saccharum ... D45997, RICS10346A Rice cDNA, partial sequence (S10346 1A). AA955567, AA955567 UI-R-E1-fa-a-08-0-UI.s1 UI-R-E1 Rattus nor... 36 3.6 AA800634, AA800634 EST190131 Normalized rat lung, Bento Soare... 36 3.6 AA660859, AA660859 00754 MtRHE Medicago truncatula cDNA 5' si... 36 3.6 AA800635, AA800635 EST190132 Normalized rat lung, Bento Soare... 36 3.6 D46069, RICS10475A Rice cDNA, partial sequence (S10475 1A). 36 3.6 H32878, H32878 EST108396 Rat PC-12 cells, untreated Rattus sp...

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Z99297, HS262D12 Homo sapiens DNA sequence from PAC 262D12 o... 1963 0.0 Z81540, CEF46B3 Caenorhabditis elegans cosmid F46B3, complet... 40 0.89 U67488, U67488 Methanococcus jannaschii section 30 of 150 of ... 38 3.5 AE000786, AE000786 Borrelia burgdorferi plasmid lp28-2, compl... 38 3.5 L02053, OMMGSHTR1 Ommastrephes sloani glutathione transferase... 38 3.5 AC004521, ATAC004521 Arabidopsis thaliana chromosome II BAC F... 38 3.5 L41250, DROGPDHN Drosophila nebulosa glycerol-3-phosphate deh... 38 3.5 AE000619, HPAE000619 Helicobacter pylori section 97 of 134 of... 38 3.5 U39720, Mycoplasma genitalium ackA, licA, mucB, rpL10, rpL32... 38 3.5 AC004533, HUAC004533 Homo sapiens Chromosome 16 BAC clone CIT... 38 3.5 U62292, HSU62292 Human elastin (ELN) gene, partial cds 38 3.5

# **HUMAN ESTs**

W02630, W02630 za52c02.rl Soares fetal liver spleen 1NFLS Hom... 1009 0.0
AA557183, AA557183 nl74f12.sl NCI\_CGAP\_Br2 Homo sapiens cDNA ... 874 0.0
AA761171, AA761171 nz09e11.sl NCI\_CGAP\_GCB1 Homo sapiens cDNA... 866 0.0
AA976975, AA976975 oq26g11.sl NCI\_CGAP\_GC4 Homo sapiens cDNA ... 854 0.0
AA449515, AA449515 zx06b11.rl Soares total fetus Nb2HF8 9w Ho... 848 0.0

AA678392, AA678392 zi26h10.s1 Soares fetal liver spleen 1NFLS... 848 0.0 AA909198, AA909198 ol12d06.s1 Soares NFL\_T\_GBC\_S1 Homo sapien... 831 0.0 W79208, W79208 zd79g05.rl Soares fetal heart NbHH19W Homo sap... 813 0.0 W03125, W03125 za53c02.rl Soares fetal liver spleen 1NFLS Hom... 807 0.0 W94750, W94750 ze13h08.rl Soares fetal heart NbHH19W Homo sap... 785 0.0 AA354894, AA354894 EST63217 Jurkat T-cells V Homo sapiens cDN... 771 0.0 H70075, H70075 yr92b03.rl Homo sapiens cDNA clone 212717 5'. W77859, W77859 zd70b08.rl Soares fetal heart NbHH19W Homo sap... 728 0.0 AA425424, AA425424 zw48f03.s1 Soares total fetus Nb2HF8 9w Ho... 718 0.0 AA476893, AA476893 zu29f09.r1 Soares ovary tumor NbHOT Homo s... 688 0.0 AA456676, AA456676 aa01h02.s1 Soares NhHMPu S1 Homo sapiens c... 688 0.0 AA662309, AA662309 nu97c11.s1 NCI\_CGAP\_Pr22 Homo sapiens cDNA... 668 0.0 W72135, W72135 zd70b08.s1 Soares fetal heart NbHH19W Homo sap... 650 0.0 N74362, N74362 za52c02.s1 Homo sapiens cDNA clone 296162 3'. 622 e-176 N66917, N66917 za47d09.s1 Homo sapiens cDNA clone 295697 3'. 585 e-165 AA251287, AA251287 zs04c06.s1 NCI\_CGAP\_GCB1 Homo sapiens cDNA... 583 e-164 AA971082, AA971082 op70h01.s1 Soares\_NFL\_T\_GBC\_S1 Homo sapien... 567 e-160 W78165, W78165 zd79g05.s1 Soares fetal heart NbHH19W Homo sap... 565 e-159 AA253290, AA253290 zr71g03.rl Soares NhHMPu S1 Homo sapiens c... 559 e-157 AA729063, AA729063 nw22f08.s1 NCI\_CGAP\_GCB0 Homo sapiens cDNA... 557 e-157 AA987313, AA987313 or81h06.s1 NCI\_CGAP\_Lu5 Homo sapiens cDNA ... 553 e-155 AA300954, AA300954 EST13832 Testis tumor Homo sapiens cDNA 5'... 541 e-152 AA425594, AA425594 zw48f03.r1 Soares total fetus Nb2HF8 9w Ho... 529 e-148 N24014, N24014 yx87g10.s1 Homo sapiens cDNA clone 268770 3'. 523 e-146 AA947355, AA947355 od86e12.s1 NCI\_CGAP Ov2 Homo sapiens cDNA ... 504 e-140 AA121074, AA121074 zl88b06.s1 Stratagene colon (#937204) Homo... 460 e-127 AA742964, AA742964 ny15d01.s1 NCI\_CGAP GCB1 Homo sapiens cDNA... 454 e-126 AA306814, AA306814 EST177885 Colon carcinoma (HCC) cell line ... 452 e-125 W87699, W87699 zh65b11.rl Soares fetal liver spleen 1NFLS S1 ... 446 e-123 W87700, W87700 zh65b11.s1 Soares fetal liver spleen 1NFLS S1 ... 438 e-121 AA449084, AA449084 zx06b11.s1 Soares total fetus Nb2HF8 9w Ho... 398 e-109 N99231, N99231 zb76f11.s1 Soares senescent fibroblasts NbHSF ... 391 e-106 N49900, N49900 yv24d04.s1 Homo sapiens cDNA clone 243655 3'. 383 e-104 AA782911, AA782911 ai62a10.s1 Soares testis NHT Homo sapiens ... 365 6e-99 AA936553, AA936553 on23g11.s1 NCI\_CGAP\_Lu5 Homo sapiens cDNA ... 361 9e-98 N74414, N74414 za53c02.s1 Homo sapiens cDNA clone 296258 3'. 353 2e-95 AA834628, AA834628 od98a10.s1 NCI\_CGAP\_Ov2 Homo sapiens cDNA ... 341 8e-92 AA693756, AA693756 zi55f11.s1 Soares fetal liver spleen 1NFLS... 341 8e-92 AA909616, AA909616 ol09d06.s1 Soares\_NFL\_T\_GBC\_S1 Homo sapien... 341 8e-92 H69662, H69662 yr92b03.s1 Homo sapiens cDNA clone 212717 3'. AA249558, AA249558 jj7521.seq.F Human fetal heart, Lambda ZAP... 317 1e-84 AA911960, AA911960 oh88g08.s1 NCI\_CGAP Co8 Homo sapiens cDNA ... 317 1e-84 AA969099, AA969099 op55e06.s1 Soares\_NFL T\_GBC S1 Homo sapien... 303 2e-80 AA766191, AA766191 oa12g08.s1 NCI\_CGAP GCB1 Homo sapiens cDNA... 212 5e-53 AA689312, AA689312 nx05e10.s1 NCI\_CGAP GC3 Homo sapiens cDNA ... 200 2e-49

AA418586, AA418586 zv93e05.rl Soares NhHMPu S1 Homo sapiens c... 182 5e-44 AA418570, AA418570 zv93e05.s1 Soares NhHMPu S1 Homo sapiens c... 182 5e-44 AA534939, AA534939 nf82f03.s1 NCI\_CGAP\_Co3 Homo sapiens cDNA ... 167 3e-39 AA888430, AA888430 nw74e05.s1 NCI\_CGAP\_Pr12 Homo sapiens cDNA... 167 3e-39 N50003, N50003 yv24d04.rl Homo sapiens cDNA clone 243655 5' s... 149 6e-34 AA535102, AA535102 nf84f06.s1 NCI\_CGAP\_Co3 Homo sapiens cDNA ... 135 1e-29 AA262335, AA262335 zr71g03.s1 Soares NhHMPu S1 Homo sapiens c... 129 6e-28 AA766681, AA766681 oa34c05.s1 NCI\_CGAP\_GCB1 Homo sapiens cDNA... 105 9e-21 AA761492, AA761492 nz27a05.s1 NCI\_CGAP\_GCB1 Homo sapiens cDNA... 101 1e-19 AA688350, AA688350 nv15a05.s1 NCI\_CGAP\_Pr22 Homo sapiens cDNA... 90 5e-16 AA347041, AA347041 EST53285 Fetal heart II Homo sapiens cDNA ... 76 8e-12 T94395, T94395 ye35e02.s1 Homo sapiens cDNA clone 119738 3'. 46 0.007 AA833565, AA833565 aj46a02.s1 Soares testis NHT Homo sapiens ... 46 0.007 AA095460, AA095460 14630.seq.F Fetal heart, Lambda ZAP Expres... 40 0.43 AA904415, AA904415 ok07e06.s1 Soares\_NFL\_T\_GBC\_S1 Homo sapien... 40 0.43 AI018800, AI018800 ov32h04.x1 Soares\_testis\_NHT Homo sapiens ... 38 1.7 AA631083, AA631083 nq77e07.s1 NCI\_CGAP\_Pr22 Homo sapiens cDNA... 38 1.7

AA399772, AA399772 vd70g05.rl Beddington mouse embryonic regi... 347 5e-94 AA467106, AA467106 vd98b04.r1 Soares mouse NbMH Mus musculus ... 309 1e-82 AI046844, AI046844 uh55c11.r1 Soares mouse embryonic stem cel... 208 3e-52 AA475075, AA475075 vh11g05.r1 Soares mouse mammary gland NbMM... 194 4e-48 AA646094, AA646094 vs31e06.r1 Stratagene mouse Tcell 937311 M... 186 1e-45 AA390020, AA390020 vb30e07.rl Soares mouse lymph node NbMLN M... 170 6e-41 AA245553, AA245553 my52g04.r1 Barstead mouse pooled organs MP... 170 6e-41 AA930741, AA930741 vs57b02.r1 Stratagene mouse skin (#937313)... 155 4e-36 W62610, W62610 md58c06.r1 Soares mouse embryo NbME13.5 14.5 M... 117 8e-25 AA239270, AA239270 my40e01.rl Barstead mouse pooled organs MP... 109 2e-22 AA015148, AA015148 mh16e01.rl Soares mouse placenta 4NbMP13.5... 54 1e-05 AA764095, AA764095 vw09h02.rl Soares 2NbMT Mus musculus cDNA ... 38 0.61 AA238570, AA238570 my35h02.r1 Barstead mouse pooled organs MP... 38 0.61 AA600576, AA600576 vm75f08.rl Knowles Solter mouse blastocyst... 38 0.61 AA636273, AA636273 vq76a10.s1 Knowles Solter mouse 2 cell Mus... 36 2.4 AA051407, AA051407 mj41f08.rl Soares mouse embryo NbME13.5 14... 36 2.4 AA823136, AA823136 vw41b03.r1 Soares mouse mammary gland NbMM... W83831, W83831 mf26a06.r1 Soares mouse embryo NbME13.5 14.5 M... 36 2.4 D77944, MUSC0D06 Mouse embryonal carcinoma F9 cell cDNA, C0D06 36 2.4 AA915408, AA915408 vz29h04.r1 Soares 2NbMT Mus musculus cDNA ... 36 2.4 AI047229, AI047229 uh63a09.r1 Soares mouse embryonic stem cel... 36 2.4 AA271880, AA271880 va73d01.r1 Soares mouse 3NME12 5 Mus muscu... AA475165, AA475165 vg95f01.rl Barstead mouse pooled organs MP... 36 2.4 AA619774, AA619774 vl58a05.s1 Knowles Solter mouse 2 cell Mus... 36 2.4

AA673116, AA673116 vn49g11.rl Barstead mouse myotubes MPLRB5 ... 36 2.4
AA870623, AA870623 vq24a07.rl Barstead stromal cell line MPLR... 36 2.4
W58907, W58907 md52f12.rl Soares mouse embryo NbME13.5 14.5 M... 36 2.4
AA690593, AA690593 vu53d05.rl Soares mouse mammary gland NbMM... 36 2.4
AA754801, AA754801 vu21f03.rl Barstead mouse myotubes MPLRB5 ... 36 2.4
AA271607, AA271607 va72a12.rl Soares mouse 3NME12 5 Mus muscu... 36 2.4
AA064256, AA064256 mj66a03.rl Soares mouse p3NMF19.5 Mus musc... 36 2.4
AA475144, AA475144 vg95d01.rl Barstead mouse pooled organs MP... 36 2.4
AA197736, AA197736 mv02g08.rl GuayWoodford Beier mouse kidney... 36 2.4

AA817944, AA817944 UI-R-A0-ag-e-01-0-UI.s1 UI-R-A0 Rattus nor... 40 0.14 F14714, SSC8B01 S.scrofa mRNA; expressed sequence tag (5'; c... 38 0.54 H91505, H91505 SWMFCA089SK Brugia malayi microfilaria cDNA (S... 36 2.1 AA998610, AA998610 UI-R-C0-if-c-04-0-UI.s1 UI-R-C0 Rattus nor... 36 2.1 AA893562, AA893562 EST197365 Normalized rat liver, Bento Soar... 36 2.1 AI008397, AI008397 EST202848 Normalized rat embryo, Bento Soa... 36 2.1

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Z92544, HS313D11 Human DNA sequence from cosmid 313D11 from ... 700 0.0 Z46940, HSPRMTNP2 H.sapiens PRM1 gene, PRM2 gene and TNP2 gene U85039, TMU85039 Theileria mutans 32 kDa immunodominant pirop... 42 0.19 U85251, TMU85251 Theileria mutans 32 kDa immunodominant pirop... 42 0.19 AF003630, AF003630 Theileria mutans clone 15, 32 kDa immunodo... 42 0.19 AF003629, AF003629 Theileria mutans clone 9, 32 kDa immunodom... 42 0.19 AB007884, AB007884 Homo sapiens KIAA0424 mRNA, partial cds 42 0.19 U85040, TMU85040 Theileria mutans 32 kDa immunodominant pirop... 42 0.19 Z97343, ATFCA8 Arabidopsis thaliana DNA chromosome 4, ESSA I... 40 0.75 L19655, TOSRNA1X Tomato ringspot virus polyprotein (RNA-1) ge... 40 0.75 M73822, TOSRNA1A Tomato ringspot virus RNA1 gene, 5' end. 40 0.75 L02543, BOVMTNNT Bos taurus nicotinamide nucleotide transhydr... 40 0.75 J03534, BOVNAD Bovine mitochondrial nicotinamide nucleotide t... 40 0.75 M62862, TRBRTE Trypanosoma cruzi retrotransposon encoding gag... 40 0.75 X72711, MMREPCFC M.musculus mRNA for replication factor C, 1... 38 3.0 M88489, MUSNBP Mus musculus nonamer binding protein mRNA, com... U36441, MMU36441 Mus musculus differentiation specific elemen... 38 3.0 AB002354, AB002354 Human mRNA for KIAA0356 gene, complete cds J03149, CATFMSC Cat (F.domesticus) c-fms proto-oncogene mRNA ... 38 3.0 J05475, CHKVICOLL Chicken type VI collagen alpha 2 (VI) subun... 38 3.0

AF038163, AF038163 Homo sapiens interleukin-15 (IL-15) gene, 38 3.0
X75917, HSFBMBF H.sapiens mRNA for fetal beta-MHC binding fa 38 3.0
X06542, DMHSPG3 Drosophila heat shock gene 3 from 67B locus 38 3.0
D17315, DRODAGK Fruit fly mRNA for diacylglycerol kinase, co 38 3.0
Z58600, HS45E3F H.sapiens CpG DNA, clone 45e3, forward read 38 3.0
D78638, D78638 Xenopus laevis mRNA for DNA (cytosine-5-)-met 38 3.0
Z49204, MMNADPTRH M.musculus mRNA for NADP transhydrogenase. 38 3.0
L10425, BPEMETC Bordetella avium beta-cystathionase-lyase (me 38 3.0
U01222, U01222 Mus musculus activator 1 large subunit (A1-p14 38 3.0
U15037, MMU15037 Mus musculus replication factor C large subu 38 3.0
K01643, FCSSMONC Feline sarcoma virus (McDonough strain) tran 38 3.0
Z57538, HS183C6F H.sapiens CpG DNA, clone 183c6, forward rea 38 3.0
U07157, MMU07157 Mus musculus ISRE-binding protein (IBF-1) mR 38 3.0
Z64961, HS183F7R H.sapiens CpG DNA, clone 183f7, reverse rea 38 3.0

#### **HUMAN ESTs**

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AF039693, AF039693 Homo sapiens unknown protein mRNA, complet... 916 0.0
S51239, S51239 calreticulin [Aplysia californica=marine snail... 48 0.005
Z74035, CEF47G9 Caenorhabditis elegans cosmid F47G9, complet... 46 0.019
AF022814, AF022814 Fugu rubripes transcription factor (SLP-1)... 44 0.073
X82638, CSCYTOX C.sordelii cytotoxin gene
U63063, SCU63063 Saccharomyces cerevisiae something about sil... 42 0.29
X63501, SCRPC53 S.cerevisiae RPC53 gene for RNA polymerase C... 42 0.29
U67572, U67572 Methanococcus jannaschii section 114 of 150 of... 42 0.29
Z74201, SCYDL153C S.cerevisiae chromosome IV reading frame O... 42 0.29
U66032, MTU66032 Methanosarcina thermophila CO dehydrogenase/... 42 0.29
Z95620, SPBC3D6 S.pombe chromosome II cosmid c3D6
                                                              42 0.29
X97751, SCIV23 S.cerevisiae chrIV genes STE7, CLB3, MSH5, RP... 42 0.29
X65541, ATCAN A.thaliana mRNA for carbonic anhydrase
                                                              42 0.29
L14750, ATHCARANHY Arabidopsis thaliana carbonic anhydrase ge... 42 0.29
U00995, U00995 Rattus norvegicus TA1 mRNA, complete cds.
                                                               40 1.1
S73876, S73876 FPR3=FKBP-70 [Saccharomyces cerevisiae, Genomi... 40 1.1
U12825, SCU12825 Saccharomyces cerevisiae transcription facto... 40 1.1
Z74237, SCYDL189W S.cerevisiae chromosome IV reading frame O... 40 1.1
U76906, REU76906 Rhizobium etli FixK (fixK), FixN (fixN), mon... 40 1.1
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AF050157, MMHC135G15 Mus musculus major histocompatibility lo 40 1.1
X58857, SCPPH22 S.cerevisiae PPH22 gene for protein phosphat 40 1.1
X79379, SCPROIS S.cerevisiae gene for proline isomerase 40 1.1
Z68341, CEF01G4 Caenorhabditis elegans cosmid F01G4, complet 40 1.1
M17192, MUSHOX1 Mouse homeodomain protein (Hox1.1) mRNA, comp 40 1.1
U50307, CELF43H9 Caenorhabditis elegans cosmid F43H9. 40 1.1
S73144, S73144 bone sialoprotein [cattle, fetal bone cells, m 40 1.1
L34569, YSCFPR3A Saccharomyces cerevisiae (clone pBYNG1) prol 40 1.1
D78303, D78303 Rattus norvegicus YT521 mRNA for RNA splicing 40 1.1
X83276, SCDNAIV S.cerevisiae DNA for ORFs from chromosome IV 40 1.1
U54558, HSU54558 Human translation initiation factor eIF3 p66 40 1.1
Z50109, CEC09H10 Caenorhabditis elegans cosmid C09H10, compl 40 1.1
X56983, EAVATP1 E.arvense gene for catalytic 70kDa V-ATPase 40 1.1
AB011125, AB011125 Homo sapiens mRNA for KIAA0553 protein, p 40 1.1
Z46373, SC8248 S.cerevisiae chromosome XIII cosmid 8248 40 1.1
AF039042, CELZK697 Caenorhabditis elegans cosmid ZK697 40 1.1
Z28028, SCYKL028W S.cerevisiae chromosome XI reading frame O 40 1.1
AC005266, AC005266 Homo sapiens chromosome 19, cosmid F23465, 38 4.5
U60822, HSU60822 Human dystrophin (DMD) gene, exons 7, 8 and 38 4.5
AJ003141, HVAJ3141 Hordeum vulgare mRNA for stress-related p 38 4.5
M26250, CRAGAP43 Goldfish (C.auratus) growth-associated prote 38 4.5
X95267, GGRYR3 G.gallus mRNA for ryanodine receptor type 3 38 4.5
L37092, MUSCDPK Mus musculus cyclin-dependent kinase homologu 38 4.5
Z72507, CEF17C11 Caenorhabditis elegans cosmid F17C11, compl 38 4.5
U29608, DMU29608 Drosophila melanogaster large tumor suppress 38 4.5
Z49072, CET24A11 Caenorhabditis elegans cosmid T24A11, compl 38 4.5
M83142, RATBGASTR Rattus norvegicus beta-galactoside-alpha 2, 38 4.5
Z20656, HSCAMHCA Homo sapiens of cardiac alpha-myosin heavy 38 4.5
M82937, YSACS2A Candida albicans chitin synthase 2 (CHS2) gen 38 4.5
U28888, MMU28888 Mus musculus neurogenic differentiation fact 38 4.5
S66408, S66408 c-erbB=proto-oncogene {exon 1, promoter} [chic 38 4.5
AC002396, AC002396 Arabidopsis thaliana chromosome I BAC F3I6 38 4.5
AE000665, MMAE000665 Mus musculus TCR beta locus from bases 5 38 4.5
L39837, DROWARTS Drosophila melanogaster tumor supressor (war 38 4.5
AG000377, AG000377 Homo sapiens genomic DNA, 21q region, clo 38 4.5
X05632, HSMHCAG1 Human alpha-MHC gene for myosin heavy chain 38 4.5
AC002108, AC002108 Genomic sequence from Mouse 4, complete se 38 4.5
U37219, HSU37219 Human cyclophilin-like protein CyP-60 mRNA, 38 4.5
M58633, MUSP58GTA Mouse p58/GTA protein kinase mRNA, complete 38 4.5
M25162, HUMMYHC08 Human cardiac alpha-myosin heavy chain (MYH 38 4.5
Z46259, SCRPD3COS S.cerevisiae FY1676 RPD3 gene. 38 4.5
U09558, LJU09558 Lactobacillus johnsonii ATCC 11506 insertion 38 4.5
U66160, MMUSC104 Mus musculus extracellular matrix associated 38 4.5
Z73126, SCYLL021W S.cerevisiae chromosome XII reading frame 38 4.5
U83981, HSU83981 Homo sapiens apoptosis associated protein (G., 38 4.5

U59897, MRU59897 Macropus robustus hypoxanthine phosphoribosy 38 4.5
D38256, YSCSCT1 Yeast gene for suppressor of ctr mutation 38 4.5
X69838, HSG9A H.sapiens mRNA for G9a 38 4.5
X52952, RNCMOSO Rat mRNA for c-mos 38 4.5
U37221, HSU37221 Human cyclophilin-like protein mRNA, partial 38 4.5
X65880, DPRH4OP1 D.pseudoobscura rh4 opsin gene, exon 1 38 4.5
U58971, NTU58971 Nicotiana tabacum calmodulin-binding protein 38 4.5
Z35773, SCYBL012C S.cerevisiae chromosome II reading frame O 38 4.5
X67668, MMHMG2 M.musculus mRNA for high mobility group 2 pro 38 4.5
L81727, HSL81727 Homo sapiens (subclone 1_d5 from P1 H69) DNA 38 4.5
AL023800, HS833B2 Human DNA sequence *** SEQUENCING IN PROGR 38 4.5
X62438, HVPERO H.vulgare mRNA for peroxidase 38 4.5
AC004096, AC004096 Mouse Cosmid ma66a100 from 14D1-D2, comple 38 4.5
AL008980, PFSC03050 Plasmodium falciparum DNA *** SEQUENCING 38 4.5
U64827, MMU64827 Mus musculus extracellular matrix associated 38 4.5
AC003010, HUAC003010 Homo sapiens Chromosome 16 BAC clone CIT 38 4.5
AE001002, AE001002 Archaeoglobus fulgidus section 105 of 172 38 4.5
U86662, LEU86662 Lycopersicon esculentum VPS41 (tVPS41) mRNA, 38 4.5
M20386, CHKEGFR Chicken epidermal growth factor receptor (CER 38 4.5
M77637, CHKEGF Gallus gallus EGF/TGF-alpha receptor (c-erbB) 38 4.5
U08185, MMU08185 Mus musculus BALB/c zinc-finger protein Blim 38 4.5
AC004231, AC004231 Homo sapiens chromosome 17, clone hRPC.111 38 4.5
Z50100, HVC39SAT H.vulgare GAA-satellite DNA 38 4.5
X53731, SCSPA2G S. cerevisiae SPA2 gene 38 4.5
U37220, HSU37220 Human cyclophilin-like protein mRNA, partial 38 4.5
X97560, SC32KBF S.cerevisiae 32kb DNA fragment of chromosome 38 4.5
AB011479, AB011479 Arabidopsis thaliana genomic DNA, chromos 38 4.5
U89340, LVU89340 Lytechinus variegtus Endo16 homolog (LvEndo1 38 4.5
U73850, TCU73850 Trypanosoma cruzi 29 kDa proteasome subunit 38 4.5
AB006698, AB006698 Arabidopsis thaliana genomic DNA, chromos 38 4.5
D37888, CYIMYC2 Cyprinus carpio c-myc gene for c-Myc, comple 38 4.5
AF017349, MMDSGIII 7 Mus musculus desmoglein 3 (Dsg3) gene, i 38 4.5
X91807, OSTA136 O.sativa mRNA for alpha-tubulin (clone OSTA 38 4.5
Z71587, SCYNL311C S.cerevisiae chromosome XIV reading frame 38 4.5
AE000742, AE000742 Aquifex aeolicus section 74 of 109 of the 38 4.5

# **HUMAN ESTs**

AA324311, AA324311 EST27136 Cerebellum II Homo sapiens cDNA 5... 593 e-167 AA639190, AA639190 ns04a01.rl NCI\_CGAP\_Ew1 Homo sapiens cDNA ... 513 e-143 AA172199, AA172199 zo96a06.rl Stratagene ovarian cancer (#937... 505 e-141 AA588066, AA588066 nk10d08.sl NCI\_CGAP\_Co2 Homo sapiens cDNA ... 502 e-140 AA412036, AA412036 zt68d09.sl Soares testis NHT Homo sapiens ... 502 e-140 AA508745, AA508745 ni23a03.sl NCI\_CGAP\_Co4 Homo sapiens cDNA ... 502 e-140

AA480337, AA480337 ne33a03.s1 NCI\_CGAP\_Co3 Homo sapiens cDNA ... 502 e-140 AA902270, AA902270 ok69e04.s1 NCI\_CGAP\_GC4 Homo sapiens cDNA ... 502 e-140 AA947303, AA947303 ok20d04.s1 Soares\_NSF\_F8\_9W\_OT\_PA\_P\_S1 Hom... 502 e-140 R23642, R23642 yh35e03.r1 Homo sapiens cDNA clone 131740 5'. 490 e-136 AA811913, AA811913 ob51d06.s1 NCI\_CGAP\_GCB1 Homo sapiens cDNA... 464 e-128 AA172083, AA172083 zo96a06.s1 Stratagene ovarian cancer (#937... 464 e-128 AA725458, AA725458 ai16g01.s1 Soares parathyroid tumor NbHPA ... 400 e-109 R26558, R26558 yh35e02.s1 Homo sapiens cDNA clone 131738 3'. 359 5e-97 AA402403, AA402403 zt68d09.r1 Soares testis NHT Homo sapiens ... 315 6e-84 R58372, R58372 G3243 Fetal heart Homo sapiens cDNA clone G324... 262 8e-68 AA389703, AA389703 M421 Fetal heart, Lambda ZAP Express Homo ... 202 6e-50 W25749, W25749 11b4 Human retina cDNA randomly primed sublibr... 103 4e-20 W27158, W27158 22h9 Human retina cDNA randomly primed sublibr... 66 1e-08 T65784, T65784 yc11f10.s1 Homo sapiens cDNA clone 80395 3' si... 42 0.14 AA179601, AA179601 zp49f10.r1 Stratagene HeLa cell s3 937216 ... 42 0.14 AA928679, AA928679 on48e08.s1 NCI\_CGAP Co8 Homo sapiens cDNA ... 40 0.55 AA887972, AA887972 nq95g11.s1 NCI\_CGAP\_Co10 Homo sapiens cDNA... 40 0.55 W46946, W46946 zc40c05.s1 Soares senescent fibroblasts NbHSF ... 40 0.55 AA887862, AA887862 nq99b08.s1 NCI\_CGAP\_Co10 Homo sapiens cDNA... 40 0.55 AA554819, AA554819 ni34d08.s1 NCI\_CGAP\_Lu1 Homo sapiens cDNA ... 40 0.55 AA557362, AA557362 nl81d12.s1 NCI\_CGAP\_Br2 Homo sapiens cDNA ... 40 0.55 AA252258, AA252258 zr29e04.s1 Stratagene NT2 neuronal precurs... 40 0.55 N34310, N34310 yy52b10.s1 Homo sapiens cDNA clone 277147 3' s... 40 0.55 AA552228, AA552228 nk06b04.s1 NCI\_CGAP\_Co2 Homo sapiens cDNA ... 40 0.55 AI017648, AI017648 ou99b02.x1 NCI CGAP Kid3 Homo sapiens cDNA... 40 0.55 T17395, T17395 NIB846 Normalized infant brain, Bento Soares H... 40 0.55 AA219659, AA219659 zr05e10.s1 Stratagene NT2 neuronal precurs... 40 0.55 AA463841, AA463841 zx67f06.rl Soares total fetus Nb2HF8 9w Ho... 40 0.55 N66817, N66817 za09b11.s1 Homo sapiens cDNA clone 292029 3' s... 40 0.55 AA167358, AA167358 zp06f12.s1 Stratagene ovarian cancer (#937... 40 0.55 AA063505, AA063505 zf70d02.rl Soares pineal gland N3HPG Homo ... 40 0.55 AA731625, AA731625 nw64a04.s1 NCI\_CGAP\_GCB1 Homo sapiens cDNA... 40 0.55 AA100119, AA100119 zl80g04.s1 Stratagene colon (#937204) Homo... 40 0.55 AA181572, AA181572 zp51d04.s1 Stratagene HeLa cell s3 937216 ... 40 0.55 AA327182, AA327182 EST30459 Colon I Homo sapiens cDNA 5' end ... 40 0.55 R48608, R48608 yj65f07.s1 Homo sapiens cDNA clone 153637 3' s... 40 0.55 AA678485, AA678485 ah06e04.s1 Gessler Wilms tumor Homo sapien... 40 0.55 AA082353, AA082353 zn38c11.rl Stratagene endothelial cell 937... 40 0.55 AA633213, AA633213 nq57c06.s1 NCI\_CGAP\_Co9 Homo sapiens cDNA ... 40 0.55 W38410, W38410 zc77g09.s1 Pancreatic Islet Homo sapiens cDNA ... 40 0.55 AA345893, AA345893 EST51967 Gall bladder I Homo sapiens cDNA ... 40 0.55 N26876, N26876 yx97f06.s1 Homo sapiens cDNA clone 269699 3' s... 40 0.55 N95279, N95279 zb60c09.s1 Soares fetal lung NbHL19W Homo sapi... 40 0.55 AI041637, AI041637 ox92h08.x1 Soares\_senescent\_fibroblasts\_Nb... 40 0.55 N67830, N67830 za05d12.s1 Homo sapiens cDNA clone 291671 3' s... 40 0.55

AA535094, AA535094 nf84e06.s1 NCI\_CGAP\_Co3 Homo sapiens cDNA ... 40 0.55 AA514414, AA514414 nf57d11.sl NCI\_CGAP Co3 Homo sapiens cDNA ... 40 0.55 T56802, T56802 ya71h07.s2 Homo sapiens cDNA clone 67165 3' co... 40 0.55 N68147, N68147 yz55f12.s1 Homo sapiens cDNA clone 286991 3' s... 40 0.55 AA535811, AA535811 nf93g10.sl NCI\_CGAP\_Co3 Homo sapiens cDNA ... 40 0.55 AA115591, AA115591 zl05g09.s1 Soares pregnant uterus NbHPU Ho... 40 0.55 N75851, N75851 za96g11.s1 Homo sapiens cDNA clone 300452 3'. 40 0.55 AA534433, AA534433 nf80a08.s1 NCI\_CGAP\_Co3 Homo sapiens cDNA ... 40 0.55 H99778, H99778 yx36g01.s1 Homo sapiens cDNA clone 263856 3' s... 40 0.55 AA970859, AA970859 oo81h03.s1 NCI\_CGAP Kid5 Homo sapiens cDNA... 40 0.55 F02131, HSC0PF092 H. sapiens partial cDNA sequence; clone c-... 40 0.55 AA810279, AA810279 od14g11.s1 NCI\_CGAP\_GCB1 Homo sapiens cDNA... 40 0.55 AA595146, AA595146 nl84b01.sl NCI\_CGAP\_Br2 Homo sapiens cDNA ... 40 0.55 AA632386, AA632386 np67e06.s1 NCI\_CGAP Br2 Homo sapiens cDNA ... 40 0.55 AA135124, AA135124 zo24c04.s1 Stratagene colon (#937204) Homo... 40 0.55 AA143500, AA143500 zo31b10.s1 Stratagene colon (#937204) Homo... AA854992, AA854992 aj53g12.s1 Soares testis NHT Homo sapiens ... 40 0.55 AA156872, AA156872 zl20h07.s1 Soares pregnant uterus NbHPU Ho... 40 0.55 AA160994, AA160994 zq41c12.s1 Stratagene hNT neuron (#937233)... 40 0.55 AA961724, AA961724 or60a10.s1 NCI\_CGAP GC3 Homo sapiens cDNA ... 40 0.55 AA551210, AA551210 nj27e09.s1 NCI\_CGAP AA1 Homo sapiens cDNA ... 40 0.55 R44103, R44103 yg27c10.s1 Homo sapiens cDNA clone 33636 3'. 40 0.55 AA938086, AA938086 oj08h08.s1 NCI\_CGAP Mel3 Homo sapiens cDNA... 40 0.55 AA576021, AA576021 nm57d11.s1 NCI\_CGAP\_Br3 Homo sapiens cDNA ... 40 0.55 AA722725, AA722725 zg86b09.s1 Soares fetal heart NbHH19W Homo... 40 0.55 AA678948, AA678948 ah08h11.s1 Gessler Wilms tumor Homo sapien... 40 0.55 W07435, W07435 za96g11.r1 Soares fetal lung NbHL19W Homo sapi... 40 0.55 T34639, T34639 EST72167 Homo sapiens cDNA 5' end similar to s... 40 0.55 AA632245, AA632245 np67b09.s1 NCI\_CGAP\_Br2 Homo sapiens cDNA ... 40 0.55 R98701, R98701 yr31f08.s1 Homo sapiens cDNA clone 206919 3'. 40 0.55 R76418, R76418 yi58a10.s1 Homo sapiens cDNA clone 143418 3'. AI028447, AI028447 ow08b09.x1 Soares\_parathyroid tumor\_NbHPA ... AI002929, AI002929 an15e12.s1 Gessler Wilms tumor Homo sapien... 40 0.55 AA779388, AA779388 ae26a03.s1 Soares NbHFB Homo sapiens cDNA ... 40 0.55 AA776220, AA776220 ah10f02.s1 Gessler Wilms tumor Homo sapien... 40 0.55 AA815223, AA815223 oc05c04.s1 NCI\_CGAP\_GCB1 Homo sapiens cDNA... 40 0.55 W60807, W60807 zd27b08.s1 Soares fetal heart NbHH19W Homo sap... 40 0.55 AA666007, AA666007 ag71g01.s1 Gessler Wilms tumor Homo sapien... 40 0.55 AA643849, AA643849 np26f07.s1 NCI\_CGAP\_Pr22 Homo sapiens cDNA... 40 0.55 AA846740, AA846740 aj99b12.s1 Soares parathyroid tumor NbHPA ... 40 0.55 AA598498, AA598498 ae38h01.s1 Gessler Wilms tumor Homo sapien... 40 0.55 AA535972, AA535972 nf95a01.s1 NCI\_CGAP\_Co3 Homo sapiens cDNA ... 40 0.55 AA488544, AA488544 ab37g06.rl Stratagene HeLa cell s3 937216 ... 40 0.55 AA866044, AA866044 oh52g07.s1 NCI\_CGAP\_GC4 Homo sapiens cDNA ... 40 0.55 C14370, C14370 Human fetal brain cDNA 5'-end GEN-050F01 40 0.55

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AA237204, AA237204 mx18d02.rl Soares mouse NML Mus musculus c... 167 1e-39
AA563402, AA563402 vl75d08.r1 Knowles Solter mouse blastocyst... 38 0.78
AA413261, AA413261 ve52f04.r1 Beddington mouse embryonic regi... 38 0.78
AA097645, AA097645 mm36f09.rl Stratagene mouse skin (#937313)... 38 0.78
AA122578, AA122578 mn25b08.rl Beddington mouse embryonic regi... 38 0.78
AA122581, AA122581 mn25c08.rl Beddington mouse embryonic regi... 38 0.78
AA646168, AA646168 vn11e06.rl Stratagene mouse Tcell 937311 M... 36 3.1
AA200881, AA200881 mu03c09.rl Soares mouse 3NbMS Mus musculus...
AI048938, AI048938 uc84h06.y1 Sugano mouse kidney mkia Mus mu... 36 3.1
AA217675, AA217675 mv01b09.r1 Soares mouse lymph node NbMLN M...
AI006387, AI006387 ua71d09.rl Soares 2NbMT Mus musculus cDNA ... 36 3.1
AA162722, AA162722 mn42b07.rl Beddington mouse embryonic regi... 36 3.1
AA207387, AA207387 mv89a11.rl GuayWoodford Beier mouse kidney... 36 3.1
AA511382, AA511382 vg14b04.r1 Soares mouse NbMH Mus musculus ... 36 3.1
AA123112, AA123112 mn30g01.rl Beddington mouse embryonic regi... 36 3.1
AA106683, AA106683 ml83h06.rl Stratagene mouse kidney (#93731... 36 3.1
AA105882, AA105882 ml84h07.rl Stratagene mouse kidney (#93731... 36 3.1
W12171, W12171 ma59a10.rl Soares mouse p3NMF19.5 Mus musculus... 36 3.1
AA208446, AA208446 mv85e01.rl GuayWoodford Beier mouse kidney... 36 3.1
AA451370, AA451370 vf84h02.rl Soares mouse mammary gland NbMM... 36 3.1
AA244639, AA244639 mx02g12.rl Soares mouse NML Mus musculus c... 36 3.1
AA267119, AA267119 mz74d07.r1 Soares mouse lymph node NbMLN M... 36 3.1
AA561847, AA561847 vl27a12.rl Stratagene mouse Tcell 937311 M... 36 3.1
AA237313, AA237313 mx17b11.rl Soares mouse NML Mus musculus c... 36 3.1
AA145817, AA145817 mq68a12.rl Soares 2NbMT Mus musculus cDNA ... 36 3.1
AA052080, AA052080 mf69f12.rl Soares mouse embryo NbME13.5 14... 36 3.1
AA000646, AA000646 mg23f09.rl Soares mouse embryo NbME13.5 14... 36 3.1
AA510521, AA510521 vh59a05.rl Soares mouse mammary gland NbMM... 36 3.1
AI006122, AI006122 ua86h01.rl Soares mouse mammary gland NbMM... 36 3.1
AA987039, AA987039 uc74e05.x1 Sugano mouse liver mlia Mus mus... 36 3.1
W77413, W77413 me64d06.rl Soares mouse embryo NbME13.5 14.5 M... 36 3.1
AA114809, AA114809 mn17e09.rl Beddington mouse embryonic regi... 36 3.1
AA793564, AA793564 vn54c05.r1 Barstead mouse myotubes MPLRB5 ... 36 3.1
AA174537, AA174537 mt10f09.r1 Soares mouse 3NbMS Mus musculus... 36 3.1
W62181, W62181 md87d08.rl Soares mouse embryo NbME13.5 14.5 M... 36 3.1
AA272905, AA272905 va39d01.r1 Soares mouse 3NME12 5 Mus muscu... 36 3.1
AA286005, AA286005 va30e05.rl GuayWoodford Beier mouse kidney... 36 3.1
AA212823, AA212823 mw81c07.r1 Soares mouse NML Mus musculus c... 36 3.1
AA125061, AA125061 mq83d10.r1 Stratagene mouse melanoma (#937... 36 3.1
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AA519228, AA519228 TgESTzz39h02.s1 TgME49 invivo Bradyzoite c... 44 0.011

AA520185, AA520185 TgESTzz39d03.s1 TgME49 invivo Bradyzoite c... 44 0.011 AA531917, AA531917 TgESTzz48f01.rl TgME49 invivo Bradyzoite c... 44 0.011 AA519997, AA519997 TgESTzz36h03.r1 TgME49 invivo Bradyzoite c... 44 0.011 AA520811, AA520811 TgESTzz64d05.rl TgME49 invivo Bradyzoite c... 44 0.011 AA520866, AA520866 TgESTzz68e05.rl TgME49 invivo Bradyzoite c... 44 0.011 AA519844, AA519844 TgESTzz36c03.r1 TgME49 invivo Bradyzoite c... 44 0.011 AA274295, AA274295 TgESTzz24c11.sl TgME49 invivo Bradyzoite c... 44 0.011 AA520901, AA520901 TgESTzz65a05.r1 TgME49 invivo Bradyzoite c... 44 0.011 AA519829, AA519829 TgESTzz36a02.rl TgME49 invivo Bradyzoite c... AA531839, AA531839 TgESTzz47h05.r1 TgME49 invivo Bradyzoite c... 44 0.011 C70525, C70525 C.elegans cDNA clone yk409g6: 5' end, single... 44 0.011 AA520235, AA520235 TgESTzz53c06.rl TgME49 invivo Bradyzoite c... T42800, T42800 6063 Lambda-PRL2 Arabidopsis thaliana cDNA clo... 42 0.044 R29976, R29976 12581 Lambda-PRL2 Arabidopsis thaliana cDNA cl... H32045, H32045 EST106774 Rat PC-12 cells, untreated Rattus sp... 40 0.18 AA819924, AA819924 MF5MA171.AE3 S. mansoni female adult Lambd... 40 0.18 H37128, H37128 15257 Lambda-PRL2 Arabidopsis thaliana cDNA cl... T04367, T04367 414 Lambda-PRL2 Arabidopsis thaliana cDNA clon... R90528, R90528 16883 Lambda-PRL2 Arabidopsis thaliana cDNA cl... 40 0.18 AA660422, AA660422 00298 MtRHE Medicago truncatula cDNA 5' 40 0.18 U94861, RRU94861 Rattus norvegicus clone HCY3 mRNA sequence 40 0.18 F14275, ATTS5197 A. thaliana transcribed sequence; clone YBY... 38 0.69 W43730, W43730 23107 CD4-16 Arabidopsis thaliana cDNA clone H... N65025, N65025 20065 Lambda-PRL2 Arabidopsis thaliana cDNA cl... 38 0.69 AI001628, AI001628 EST0210 Tilapia brain cDNA library in pUC1... 38 0.69 H74687, H74687 383 Brassica napus cDNA clone R25R. 38 0.69 AA395597, AA395597 27394 Lambda-PRL2 Arabidopsis thaliana cDN... 38 0.69 AA753070, AA753070 97AS2091 Rice Immature Seed Lambda ZAPII c... 38 0.69 D41274, RICS3647A Rice cDNA, partial sequence (S3647 1A). 38 0.69 Z25731, ATTS1208 A. thaliana transcribed sequence; clone VCV... 38 0.69 N82780, N82780 TgESTzy34e03.rl TgRH Tachyzoite cDNA Toxoplasm... 38 0.69 AA597822, AA597822 29889 Lambda-PRL2 Arabidopsis thaliana cDN... 38 0.69 AA948906, AA948906 LD27590.5prime LD Drosophila melanogaster ... 38 0.69 AI013695, AI013695 EST208370 Normalized rat spleen, Bento Soa... 38 0.69 AA753263, AA753263 96BS0294 Rice Immature Seed Lambda ZAPII c... F14402, ATTS5324 A. thaliana transcribed sequence; clone TAP... 36 2.7 T46158, T46158 9421 Lambda-PRL2 Arabidopsis thaliana cDNA clo... C91400, C91400 Dictyostelium discoideum slug cDNA, clone SSK169 T46009, T46009 9272 Lambda-PRL2 Arabidopsis thaliana cDNA clo... 36 2.7 AA440655, AA440655 LD15510.5prime LD Drosophila melanogaster ... 36 2.7 AA559374, AA559374 MU002092.NH3 York-Harrop-lung-A Schistosom... Z32623, ATTS2751 A. thaliana transcribed sequence; clone YAP... 36 2.7 T43683, T43683 6946 Lambda-PRL2 Arabidopsis thaliana cDNA clo... 36 2.7 AA263535, AA263535 LD06645.5prime LD Drosophila melanogaster ... 36 2.7 C37095, C37095 C.elegans cDNA clone yk482c11: 3' end, singl... 36 2.7

C57017, C57017 C.elegans cDNA clone yk308h9: 3' end, single... 36 2.7 C93857, C93857 Dictyostelium discoideum slug cDNA, clone SSL794 C92242, C92242 Dictyostelium discoideum slug cDNA, clone SSD283 Z33976, ATTS3037 A. thaliana transcribed sequence; clone YAP... 36 2.7 R62091, R62091 EST351 Strongylocentrotus purpuratus cDNA 5' end. 36 2.7 AA567455, AA567455 HL01288.5prime HL Drosophila melanogaster ... 36 2.7 C74456, C74456 Rice cDNA, partial sequence (E31357 1A) AA753227, AA753227 97AS2316 Rice Immature Seed Lambda ZAPII c... 36 2.7 C92456, C92456 Dictyostelium discoideum slug cDNA, clone SSE569 T20458, T20458 2466 Lambda-PRL2 Arabidopsis thaliana cDNA clo... 36 2.7 R29905, R29905 12510 Lambda-PRL2 Arabidopsis thaliana cDNA cl... 36 2.7 M79841, M79841 wEST00378 Caenorhabditis elegans cDNA clone CE... 36 2.7 Z17562, ATTS0136 A. thaliana transcribed sequence; clone TAT... 36 2.7 D71983, CELK084H2R C.elegans cDNA clone yk84h2: 3' end, sin... 36 2.7 T20404, T20404 2412 Lambda-PRL2 Arabidopsis thaliana cDNA clo... 36 2.7 AI012789, AI012789 EST207240 Normalized rat placenta, Bento S... 36 2.7 U83048, BTU83048 Bos taurus clone 0429 mRNA sequence 36 2.7 AA660182, AA660182 00022 MtRHE Medicago truncatula cDNA 5' si... 36 2.7 D48514, RICS14740A Rice cDNA, partial sequence (S14740 1A). 36 2.7 C90110, C90110 Dictyostelium discoideum slug cDNA, clone SSI103 36 2.7 H36880, H36880 15009 Lambda-PRL2 Arabidopsis thaliana cDNA cl... 36 2.7 AA699152, AA699152 HL07807.5prime HL Drosophila melanogaster ... 36 2.7 C11922, C11922 C.elegans cDNA clone yk144a11: 5' end, singl... AA816691, AA816691 LD03795.5prime LD Drosophila melanogaster ... 36 2.7

# **SEQ ID NO:556**

X99668, MM22A3 M.musculus mRNA for exon from unknown gene 22A3 260 5e-67 Z83760, CICOS41 Ciona intestinalis DNA sequence from cosmid ... 40 0.94 Z75710, CED1081 Caenorhabditis elegans cosmid D1081, complet... U73628, HSU73628 Human chromosome 11 101h11 cosmid, complete ... 40 0.94 X99757, DMDYDTRO D.melanogaster mRNA for dystrophin U51189, HIVU51189 HIV-1 clone 93th253 from Thailand, complete... 38 3.7 AC004118, AC004118 Drosophila melanogaster (P1 DS06238 (D26))... 38 3.7 U50313, CELF44C4 Caenorhabditis elegans cosmid F44C4. 38 3.7 AC004503, AC004503 Homo sapiens chromosome 5, P1 clone 1354A7... 38 3.7 M16840, WHTCPCA2 Wheat Asp-tRNA gene. 38 3.7 Y13381, RNAMPH1 Rattus norvegicus mRNA for amphiphysin, amphl 38 3.7 AC002994, AC002994 Homo sapiens chromosome 17, clone HRPC987K... 38 3.7 AB008271, AB008271 Arabidopsis thaliana genomic DNA, chromos... 38 3.7 D49701, ASNNIAD Aspergillus oryzae niaD gene for nitrate red... 38 3.7

X59422, HSPLD1 H.sapiens Pl d1 repetitive DNA 38 3.7 Z98555, PFSC03027 Plasmodium falciparum DNA \*\*\* SEQUENCING I... 38 3.7

#### **HUMAN ESTs**

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AA315671, AA315671 EST187451 Colon carcinoma (HCC) cell line ... 932 0.0
U56653, HSU56653 Human heat shock inducible mRNA
AA487685, AA487685 ab23b09.r1 Stratagene lung (#937210) Homo ... 751 0.0
AA044797, AA044797 zk67g12.r1 Soares pregnant uterus NbHPU Ho... 749 0.0
AA314922, AA314922 EST186735 HCC cell line (matastasis to liv... 698 0.0
AA082278, AA082278 zn42d12.rl Stratagene endothelial cell 937... 668 0.0
H22613, H22613 yn64f03.rl Homo sapiens cDNA clone 173213 5'.
AA044743, AA044743 zk67g12.s1 Soares pregnant uterus NbHPU Ho... 622 e-176
AA487470, AA487470 ab23b09.s1 Stratagene lung (#937210) Homo ... 601 e-170
AA121057, AA121057 zm22b03.r1 Stratagene pancreas (#937208) H... 581 e-164
AA194396, AA194396 zq05g05.s1 Stratagene muscle 937209 Homo s... 535 e-150
AA384283, AA384283 EST97787 Thyroid Homo sapiens cDNA 5' end
AA669015, AA669015 ab88f01.s1 Stratagene lung (#937210) Homo ... 535 e-150
AA194336, AA194336 zq05g05.r1 Stratagene muscle 937209 Homo s... 505 e-141
R96173, R96173 yt84e09.r1 Homo sapiens cDNA clone 231016 5'.
AA028934, AA028934 zk08b09.s1 Soares pregnant uterus NbHPU Ho... 484 e-134
AA564849, AA564849 nj22c04.sl NCI_CGAP_AA1 Homo sapiens cDNA ... 442 e-122
AA932576, AA932576 oo57g10.s1 NCI_CGAP_Lu5 Homo sapiens cDNA ... 440 e-121
AA876265, AA876265 oi12g09.s1 NCI CGAP GC4 Homo sapiens cDNA ... 434 e-120
AA025525, AA025525 ze86a11.s1 Soares fetal heart NbHH19W Homo... 430 e-118
U56654, HSU56654 Human heat shock inducible mRNA
                                                            426 e-117
AA746600, AA746600 nx18c02.s1 NCI_CGAP_GC3 Homo sapiens cDNA ... 406 e-111
AA876346, AA876346 oj24a11.s1 NCI_CGAP Kid5 Homo sapiens cDNA... 406 e-111
W23082, W23082 78D1 Human retina cDNA Tsp509I-cleaved sublibr... 402 e-110
AI034059, AI034059 ow14h11.x1 Soares parathyroid tumor NbHPA ... 357 2e-96
AA662934, AA662934 nu92d09.s1 NCI_CGAP_Pr22 Homo sapiens cDNA... 323 2e-86
AA844331, AA844331 ai95f01.s1 Soares parathyroid tumor NbHPA ... 301 8e-80
AA249866, AA249866 y0761.seq.F Human fetal heart, Lambda ZAP ... 297 1e-78
R19215, R19215 yg24b07.r1 Homo sapiens cDNA clone 33126 5'.
                                                              280 3e-73
T39355, T39355 ya04g08.rl Homo sapiens cDNA clone 60542 5'.
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AA731264, AA731264 nw57c08.s1 NCI_CGAP_GCB1 Homo sapiens cDNA... 220 2e-55
AA768549, AA768549 oa67c07.s1 NCI_CGAP_GCB1 Homo sapiens cDNA... 220 2e-55
AA668506, AA668506 ac49a11.s1 Stratagene hNT neuron (#937233)... 216 4e-54
T55337, T55337 yb79b05.s1 Homo sapiens cDNA clone 77361 3'.
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AA860575, AA860575 aj86a09.sl Soares parathyroid tumor NbHPA ... 198 8e-49
AA335548, AA335548 EST39962 Epididymus Homo sapiens cDNA 5' end 109 6e-22
R13183, R13183 yf73f02.r1 Homo sapiens cDNA clone 27960 5'.
                                                              58 2e-06
T80034, T80034 yd04c06.r1 Homo sapiens cDNA clone 24672 5'.
AA595230, AA595230 nl84g02.s1 NCI CGAP Br2 Homo sapiens cDNA ... 38 1.8
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AA871935, AA871935 vq42h02.rl Barstead bowel MPLRB9 Mus muscu... 664 0.0 AA062330, AA062330 ml35e10.r1 Stratagene mouse testis (#93730... 589 e-167 AI048164, AI048164 ud71b09.y1 Sugano mouse liver mlia Mus mus... 537 e-151 W08037, W08037 mb37h01.r1 Soares mouse p3NMF19.5 Mus musculus... 462 e-128 AA387311, AA387311 vc19a03.rl Ko mouse embryo 11 5dpc Mus mus... 264 6e-69 AA163072, AA163072 ms31a11.rl Stratagene mouse skin (#937313)... 212 2e-53 AA596763, AA596763 vm60a10.r1 Stratagene mouse Tcell 937311 M... 178 3e-43 AA562549, AA562549 vl63a11.r1 Knowles Solter mouse blastocyst... 143 2e-32 AA212378, AA212378 mu44c03.rl Soares 2NbMT Mus musculus cDNA ... 113 1e-23 AA450862, AA450862 vg55h12.r1 Beddington mouse embryonic regi... 111 5e-23 AA990073, AA990073 ua59a01.rl Soares 2NbMT Mus musculus cDNA ... 86 3e-15 AA921175, AA921175 vy54b10.r1 Stratagene mouse lung 937302 Mu... 78 8e-13 AA261119, AA261119 mz89e01.rl Soares mouse NML Mus musculus c... 38 0.65 AI005952, AI005952 ua80f06.rl Soares 2NbMT Mus musculus cDNA ... 36 2.6 AA123274, AA123274 mn23a08.rl Beddington mouse embryonic regi... 36 2.6 AI036828, AI036828 vw96c02.r1 Stratagene mouse skin (#937313)... 36 2.6

H35787, H35787 EST109178 Rat PC-12 cells, NGF-treated (9 days... 105 3e-21 AA686082, AA686082 EST109179 Rat PC-12 cells, NGF-treated (9 ... 86 3e-15 C23464, C23464 Jpanese flounder liver cDNA, LE5(10) 72 4e-11 C23465, C23465 Jpanese flounder liver cDNA, LE5(10) 56 2e-06 AA520314, AA520314 TgESTzz38h12.r1 TgME49 invivo Bradyzoite c... 38 0.57 AA520085, AA520085 TgESTzz37g05.r1 TgME49 invivo Bradyzoite c... 38 0.57 AA520033, AA520033 TgESTzz36f10.rl TgME49 invivo Bradyzoite c... 38 0.57 AA012516, AA012516 TgESTzz23f04.rl TgME49cDNA Toxoplasma gond... AA274286, AA274286 TgESTzz24c01.s1 TgME49 invivo Bradyzoite c... 38 0.57 AA660585, AA660585 00471 MtRHE Medicago truncatula cDNA 5' si... 38 0.57 L35828, BNAESTBD Brassica rapa (clone F0621) expressed sequen... 38 0.57 AA520070, AA520070 TgESTzz37e05.r1 TgME49 invivo Bradyzoite c... 38 0.57 C30080, C30080 C.elegans cDNA clone yk236c3: 3' end, single... 36 2.3 C39044, C39044 C.elegans cDNA clone yk505a4: 3' end, single... 36 2.3 C55023, C55023 C.elegans cDNA clone yk422a3: 3' end, single... 36 2.3 AA542589, AA542589 fa08d06.s1 Zebrafish ICRFzfls Danio rerio ... 36 2.3 N25370, N25370 EST000480 Schistosoma mansoni cDNA clone SMTBA... 36 2.3 AA820625, AA820625 LD24443.5prime LD Drosophila melanogaster ... 36 2.3 AA494922, AA494922 fa12g10.r1 Zebrafish ICRFzfls Danio rerio ... 36 2.3 AA495181, AA495181 fa04d06.s1 Zebrafish ICRFzfls Danio rerio ... 36 2.3 D73287, CELK116G6R C.elegans cDNA clone yk116g6: 3' end, si... 36 2.3 C28238, C28238 Rice cDNA, partial sequence (C60429 1A) 36 2.3

#### **SEQ ID NO:557**

AF039693, AF039693 Homo sapiens unknown protein mRNA, complet... 948 0.0 S51239, S51239 calreticulin [Aplysia californica=marine snail... 56 1e-05 Z74035, CEF47G9 Caenorhabditis elegans cosmid F47G9, complet... 46 0.012 U25723, CPU25723 Cavia porcellus alpha-2B adrenoceptor gene, ... 44 0.047 AL021407, HS13D10 Homo sapiens DNA sequence from PAC 13D10 o... 42 0.19 U67572, U67572 Methanococcus jannaschii section 114 of 150 of... 42 0.19 V01470, ZMZE01 Zea mays gene encoding a zein gene (clone lam... 42 0.19 U06631, HSU06631 Human (H326) mRNA, complete cds. 42 0.19 X82638, CSCYTOX C.sordelii cytotoxin gene 42 0.19 AE000926, AE000926 Methanobacterium thermoautotrophicum from ... 42 0.19 AC004135, AC004135 Genomic sequence for Arabidopsis thaliana ... 42 0.19 AC003010, HUAC003010 Homo sapiens Chromosome 16 BAC clone CIT... 40 0.74 AF050157, MMHC135G15 Mus musculus major histocompatibility lo... 40 0.74 AC002352, AC002352 Homo sapiens 12q24 PAC P256D10 complete se... 40 0.74 X07699, MMNUCLEO Mouse nucleolin gene 40 0.74 X02399, MMHOM6 Mouse embryonal carcinoma DNA fragment contai... 40 0.74 M93661, RATNOTCHX Rat notch 2 mRNA. M17440, MUSMHC4H2S Mouse MHC (H-2) S region complement compon... U15972, MMU15972 Mus musculus homeobox (Hoxa7) gene, complete... AB001601, AB001601 Homo sapiens DBP2 mRNA for ATP-dependent ... 40 0.74 U09820, HSU09820 Human helicase II (RAD54L) mRNA, complete cds. AB011149, AB011149 Homo sapiens mRNA for KIAA0577 protein, c... 40 0.74 U26259, MMU26259 Mus musculus C2-H2 zinc finger protein mRNA,... 40 0.74 L48363, MUSZFPTR Mus musculus zinc finger protein gene, compl... 40 0.74 AC003113, AC003113 Arabidopsis thaliana BAC F24O1 chromosome ... 40 0.74 D76432, D76432 Mouse mRNA for transcriptional repressor delt... 40 0.74 U72937, HSU72937 Human putative DNA dependent ATPase and heli... 40 0.74 U72915, HSATRX16 Human putative DNA dependent ATPase and heli... U00995, U00995 Rattus norvegicus TA1 mRNA, complete cds. Z48618, SCCHVII35 S.cerevisiae genes for RAD54, ACE1(CUP2), ... 40 0.74 U75653, HSU75653 Human zinc finger helicase (Znf-HX) mRNA, co... Z72672, SCYGL150C S.cerevisiae chromosome VII reading frame ... 40 0.74 Z50109, CEC09H10 Caenorhabditis elegans cosmid C09H10, compl... 40 0.74 AF013969, AF013969 Mus musculus antigen containing epitope to... 40 0.74 M95627, HUMAAMP1X Homo sapiens angio-associated migratory cel... 40 0.74 U72936, HSU72936 Human putative DNA dependent ATPase and heli... 40 0.74 M88753, DROHTCHRPI Fruitfly heterochromatin protein-1 gene, c... 40 0.74 U76906, REU76906 Rhizobium etli FixK (fixK), FixN (fixN), mon... 40 0.74 U97085, HSXNP14 Homo sapiens X-linked nuclear protein (ATRX) ... 40 0.74 L34363, HUMNUCPRO Human X-linked nuclear protein (XNP) gene, ... 40 0.74 U72938, HSU72938 Human putative DNA dependent ATPase and heli... 40 0.74

X56983, EAVATP1 E.arvense gene for catalytic 70kDa V-ATPase ... 40 0.74 U88539, MMU88539 Mus musculus chromatin structural protein ho... 40 0.74 U07704, HSU07704 Human protein kinase PITSLRE isoform PBETA21... 38 2.9 U07705, HSU07705 Human protein kinase PITSLRE isoform PBETA22... 38 2.9 AF019612, AF019612 Homo sapiens S2P mRNA, complete cds U04818, HSU04818 Human protein kinase PITSLRE alpha 2-4 mRNA,... 38 2.9 AB002381, AB002381 Human mRNA for KIAA0383 gene, partial cds AB009520, AB009520 Pyrococcus horikoshii OT3 genomic DNA, 13... 38 2.9 Z83848, HS57A13 Human DNA sequence from PAC 57A13 between ma... 38 2.9 AC004592, AC004592 Homo sapiens PAC clone DJ0244J05 from 5q31... 38 2.9 L11710, ZEFZCMYC Brachydanio rerio c-myc oncoprotein mRNA, co... 38 2.9 D43920, CHKMETASE Chicken mRNA for DNA (cytosine-5-)-methylt... U49056, RNU49056 Rattus norvegicus CTD-binding SR-like protei... 38 2.9 U04824, HSU04824 Human protein kinase PITSLRE alpha 2-1 mRNA,... 38 2.9 U78045, HSU78045 Human collagenase and stromelysin genes, com... 38 2.9 U04816, HSU04816 Human protein kinase PITSLRE alpha 2-2 mRNA,... 38 2.9 U04817, HSU04817 Human protein kinase PITSLRE alpha 2-3 mRNA,... 38 2.9

#### **HUMAN ESTs**

AA639190, AA639190 ns04a01.rl NCI\_CGAP Ew1 Homo sapiens cDNA ... 519 e-145 AA172199, AA172199 zo96a06.rl Stratagene ovarian cancer (#937... 513 e-144 R23642, R23642 yh35e03.rl Homo sapiens cDNA clone 131740 5'. 490 e-136 AA902270, AA902270 ok69e04.s1 NCI\_CGAP\_GC4 Homo sapiens cDNA ... 450 e-124 AA947303, AA947303 ok20d04.s1 Soares\_NSF\_F8\_9W\_OT\_PA\_P\_S1 Hom... 402 e-110 AA588066, AA588066 nk10d08.s1 NCI\_CGAP\_Co2 Homo sapiens cDNA ... 347 1e-93 AA412036, AA412036 zt68d09.s1 Soares testis NHT Homo sapiens ... 347 1e-93 AA480337, AA480337 ne33a03.s1 NCI\_CGAP Co3 Homo sapiens cDNA ... 347 1e-93 AA508745, AA508745 ni23a03.s1 NCI\_CGAP Co4 Homo sapiens cDNA ... 347 1e-93 AA172083, AA172083 zo96a06.s1 Stratagene ovarian cancer (#937... 315 4e-84 AA811913, AA811913 ob51d06.s1 NCI\_CGAP\_GCB1 Homo sapiens cDNA... 299 2e-79 AA402403, AA402403 zt68d09.r1 Soares testis NHT Homo sapiens ... 299 2e-79 AA725458, AA725458 ai16g01.s1 Soares parathyroid tumor NbHPA ... 250 2e-64 R26558, R26558 yh35e02.s1 Homo sapiens cDNA clone 131738 3'. 250 2e-64 W25749, W25749 11b4 Human retina cDNA randomly primed sublibr... 103 3e-20 W27158, W27158 22h9 Human retina cDNA randomly primed sublibr... 66 6e-09 AA737681, AA737681 nw63c04.s1 NCI\_CGAP GCB1 Homo sapiens cDNA... T65784, T65784 yc11f10.s1 Homo sapiens cDNA clone 80395 3' si... 42 0.090 R52021, R52021 yg84h09.r1 Homo sapiens cDNA clone 40181 5' si... 42 0.090 AA569993, AA569993 nm47h04.s1 NCI\_CGAP\_Br2 Homo sapiens cDNA ... 42 0.090 R50149, R50149 yj61c05.s1 Homo sapiens cDNA clone 153224 3' s... 42 0.090 R87930, R87930 yo47a11.s1 Homo sapiens cDNA clone 181052 3' s... 42 0.090 AA812204, AA812204 ob84f01.s1 NCI\_CGAP\_GCB1 Homo sapiens cDNA... 42 0.090 AA770224, AA770224 ah82e12.s1 Soares testis NHT Homo sapiens ... 42 0.090

D29591, HUMNK752 Human keratinocyte cDNA, clone 752 40 0.36 AA324325, AA324325 EST27219 Cerebellum II Homo sapiens cDNA 5... 40 0.36 AA053063, AA053063 zl71c03.rl Stratagene colon (#937204) Homo... 40 0.36 T35539, T35539 EST86964 Homo sapiens cDNA 5' end similar to N... 40 0.36 AA974278, AA974278 oq14d03.s1 NCI\_CGAP\_GC4 Homo sapiens cDNA ... 40 0.36 W26196, W26196 22b5 Human retina cDNA randomly primed sublibr... 40 0.36 H92585, H92585 yt89c03.s1 Homo sapiens cDNA clone 231460 3'. 40 0.36 AA232334, AA232334 zr27b04.rl Stratagene NT2 neuronal precurs... 40 0.36 N55775, N55775 J2481F Homo sapiens cDNA clone J2481 5'. 40 0.36 R98701, R98701 yr31f08.s1 Homo sapiens cDNA clone 206919 3'. 40 0.36 C14370, C14370 Human fetal brain cDNA 5'-end GEN-050F01 40 0.36 H19156, H19156 yn50c01.rl Homo sapiens cDNA clone 171840 5'. 40 0.36 AA299557, AA299557 EST12080 Uterus tumor I Homo sapiens cDNA ... 40 0.36 W84460, W84460 zd89d12.r1 Soares fetal heart NbHH19W Homo sap... 40 0.36 T54194, T54194 ya90a02.r2 Homo sapiens cDNA clone 68906 5'. AA100203, AA100203 zm16f12.rl Stratagene pancreas (#937208) H... 38 1.4 AA993061, AA993061 ot92h08.s1 Soares total fetus Nb2HF8 9w Ho... R53406, R53406 yj70d07.r1 Homo sapiens cDNA clone 154093 5' s... 38 1.4 H99671, H99671 yx35b03.s1 Homo sapiens cDNA clone 263693 3'. 38 1.4 W03410, W03410 za07c09.r1 Soares melanocyte 2NbHM Homo sapien... 38 1.4 N35475, N35475 yy24b03.s1 Homo sapiens cDNA clone 272141 3'. 38 1.4 AA630851, AA630851 nt57f04.s1 NCI\_CGAP\_Pr3 Homo sapiens cDNA ... 38 1.4 N66458, N66458 yz41b08.s1 Homo sapiens cDNA clone 285591 3'. AA736438, AA736438 zh31b09.s1 Soares pineal gland N3HPG Homo ... 38 1.4 AA911761, AA911761 og19b01.sl NCI\_CGAP PNS1 Homo sapiens cDNA... 38 1.4 AA085513, AA085513 zn43a10.rl Stratagene HeLa cell s3 937216 ... 38 1.4 AA678530, AA678530 ah02e05.s1 Gessler Wilms tumor Homo sapien... 38 1.4 AA782011, AA782011 ai75b12.s1 Soares testis NHT Homo sapiens ... 38 1.4 F12352, HSC38H091 H. sapiens partial cDNA sequence; clone c-... 38 1.4 AA861288, AA861288 ak33g01.sl Soares testis NHT Homo sapiens ... 38 1.4 AA908705, AA908705 ol01b09.s1 NCI CGAP Lu5 Homo sapiens cDNA ... 38 1.4 AA298850, AA298850 EST114450 Thyroid Homo sapiens cDNA 5' end 38 1.4

AA237204, AA237204 mx18d02.rl Soares mouse NML Mus musculus c... 172 1e-41 AI047347, AI047347 ud65c01.yl Sugano mouse liver mlia Mus mus... 42 0.032 AA832736, AA832736 vw45g10.rl Soares mouse mammary gland NbMM... 42 0.032 AA960471, AA960471 vw63a05.sl Soares mouse mammary gland NMLM... 40 0.13 AA880584, AA880584 vw92e01.rl Stratagene mouse skin (#937313)... 40 0.13 AA107508, AA107508 mp05e07.rl Life Tech mouse embryo 8 5dpc 1... 40 0.13 AA116682, AA116682 mn28c06.rl Beddington mouse embryonic regi... 40 0.13 AA522310, AA522310 vi45b02.rl Beddington mouse embryonic regi... 40 0.13 AA162231, AA162231 mn44h02.rl Beddington mouse embryonic regi... 40 0.13

AA414037, AA414037 vc68g03.s1 Knowles Solter mouse 2 cell Mus... 40 0.13 AA596585, AA596585 vm58e12.r1 Stratagene mouse Tcell 937311 M... 38 0.51 AA863563, AA863563 vx05a10.r1 Soares 2NbMT Mus musculus cDNA ... 38 0.51 AA795177, AA795177 vq94g04.rl Knowles Solter mouse blastocyst... 38 0.51 AA914764, AA914764 vy92h04.r1 Soares mouse mammary gland NbMM... 38 0.51 AA590440, AA590440 vm20c04.rl Knowles Solter mouse blastocyst... 38 0.51 AA563402, AA563402 vl75d08.rl Knowles Solter mouse blastocyst... 38 0.51 AA260352, AA260352 va93c10.r1 Soares mouse 3NME12 5 Mus muscu... 38 0.51 AA444734, AA444734 ve75d10.r1 Soares mouse mammary gland NbMM... 38 0.51 C85885, C85885 Mus musculus fertilized egg cDNA 3'-end seque... 38 0.51 AA794590, AA794590 vu78h12.r1 Stratagene mouse skin (#937313)... 38 0.51 AA529643, AA529643 vi38a09.rl Beddington mouse embryonic regi... 38 0.51 AA607084, AA607084 vm84a09.rl Knowles Solter mouse blastocyst... 38 0.51 AA636994, AA636994 vn05g06.r1 Knowles Solter mouse blastocyst... AA675676, AA675676 vr73h08.s1 Knowles Solter mouse 2 cell Mus... 38 0.51 AA163890, AA163890 ms52f09.rl Life Tech mouse embryo 13 5dpc ... 38 0.51 C80539, C80539 Mus musculus 3.5-dpc blastocyst cDNA 3'-end s... 38 0.51 AA051352, AA051352 mj53a09.rl Soares mouse embryo NbME13.5 14... 38 0.51 W36885, W36885 mb64f09.r1 Soares mouse p3NMF19.5 Mus musculus... 38 0.51 AA930627, AA930627 vy67c05.r1 Stratagene mouse macrophage (#9... 38 0.51 AA244639, AA244639 mx02g12.rl Soares mouse NML Mus musculus c... 36 2.0 AA967267, AA967267 vz70e08.rl Soares mouse mammary gland NbMM... 36 2.0 AI048938, AI048938 uc84h06.y1 Sugano mouse kidney mkia Mus mu... 36 2.0 AA162722, AA162722 mn42b07.rl Beddington mouse embryonic regi... 36 2.0 AA170036, AA170036 ms52d01.rl Life Tech mouse embryo 13 5dpc ... 36 2.0 AA511382, AA511382 vg14b04.r1 Soares mouse NbMH Mus musculus ... 36 2.0 AA555634, AA555634 vk49f08.r1 Stratagene mouse Tcell 937311 M... 36 2.0 AA212823, AA212823 mw81c07.r1 Soares mouse NML Mus musculus c... 36 2.0 AA606813, AA606813 vm90h12.r1 Knowles Solter mouse blastocyst... 36 2.0 AA591610, AA591610 vk49d08.rl Stratagene mouse Tcell 937311 M... 36 2.0 AA987039, AA987039 uc74e05.x1 Sugano mouse liver mlia Mus mus... 36 2.0 AA105882, AA105882 ml84h07.rl Stratagene mouse kidney (#93731... 36 2.0 AA451370, AA451370 vf84h02.rl Soares mouse mammary gland NbMM... 36 2.0 AA612185, AA612185 vo03d05.r1 Stratagene mouse skin (#937313)... 36 2.0 AA103424, AA103424 mo21e05.rl Life Tech mouse embryo 13 5dpc ... 36 2.0 AA145817, AA145817 mq68a12.r1 Soares 2NbMT Mus musculus cDNA ... 36 2.0 AA272905, AA272905 va39d01.r1 Soares mouse 3NME12 5 Mus muscu... 36 2.0 AA237313, AA237313 mx17b11.rl Soares mouse NML Mus musculus c... 36 2.0 AA267119, AA267119 mz74d07.r1 Soares mouse lymph node NbMLN M... 36 2.0 AA106683, AA106683 ml83h06.rl Stratagene mouse kidney (#93731... 36 2.0 AA125061, AA125061 mq83d10.rl Stratagene mouse melanoma (#937... 36 2.0 AA655241, AA655241 vq84c07.s1 Knowles Solter mouse 2 cell Mus... 36 2.0 AA512835, AA512835 vg13f11.r1 Soares mouse NbMH Mus musculus ... 36 2.0

C70525, C70525 C.elegans cDNA clone yk409g6: 5' end, single... 44 0.007 F15112, SSO4D09 S.scrofa mRNA; expressed sequence tag (5'; c... 42 0.029 AA684640, AA684640 EST104989 Rat PC-12 cells, untreated Rattu... H32045, H32045 EST106774 Rat PC-12 cells, untreated Rattus sp... 40 0.11 AA660422, AA660422 00298 MtRHE Medicago truncatula cDNA 5' 40 0.11 C59696, C59696 C.elegans cDNA clone yk440e1: 3' end, single... 38 0.45 AI008699, AI008699 EST203150 Normalized rat embryo, Bento Soa... 38 0.45 AA753263, AA753263 96BS0294 Rice Immature Seed Lambda ZAPII c... 38 0.45 T38461, T38461 EST103957 Saccharomyces cerevisiae cDNA 3' end. 38 0.45 C59257, C59257 C.elegans cDNA clone yk386b12: 3' end, singl... 38 0.45 AA948906, AA948906 LD27590.5prime LD Drosophila melanogaster ... 38 0.45 AI001628, AI001628 EST0210 Tilapia brain cDNA library in pUC1... 38 0.45 H31962, H31962 EST106545 Rat PC-12 cells, untreated Rattus sp... 38 0.45 AA979509, AA979509 LD34118.5prime LD Drosophila melanogaster ... 38 0.45 D41274, RICS3647A Rice cDNA, partial sequence (S3647 1A). 38 0.45 C58362, C58362 C.elegans cDNA clone yk366a8: 3' end, single... 38 0.45 C57756, C57756 C.elegans cDNA clone yk298b9: 3' end, single... 38 0.45 AA753070, AA753070 97AS2091 Rice Immature Seed Lambda ZAPII c... 38 0.45 H74687, H74687 383 Brassica napus cDNA clone R25R. 38 0.45 C10513, C10513 C.elegans cDNA clone yk147e9: 3' end, single... 38 0.45 C55569, C55569 C.elegans cDNA clone yk191d1: 3' end, single... 38 0.45 C94819, C94819 Sus scrofa mRNA; expressed sequence tag (5'; ... C32982, C32982 C.elegans cDNA clone yk338a12: 3' end, singl... 38 0.45 AA816691, AA816691 LD03795.5prime LD Drosophila melanogaster ... 36 1.8 AA519844, AA519844 TgESTzz36c03.rl TgME49 invivo Bradyzoite c... 36 1.8 AA531839, AA531839 TgESTzz47h05.r1 TgME49 invivo Bradyzoite c... 36 1.8 AA660182, AA660182 00022 MtRHE Medicago truncatula cDNA 5' si... 36 1.8 D71983, CELK084H2R C.elegans cDNA clone yk84h2: 3' end, sin... 36 1.8 R29905, R29905 12510 Lambda-PRL2 Arabidopsis thaliana cDNA cl... 36 1.8 AA519997, AA519997 TgESTzz36h03.r1 TgME49 invivo Bradyzoite c... U83048, BTU83048 Bos taurus clone 0429 mRNA sequence AA440655, AA440655 LD15510.5prime LD Drosophila melanogaster ... 36 1.8 AA559374, AA559374 MU002092.NH3 York-Harrop-lung-A Schistosom... C93857, C93857 Dictyostelium discoideum slug cDNA, clone SSL794 36 1.8 AA520901, AA520901 TgESTzz65a05.r1 TgME49 invivo Bradyzoite c... 36 1.8 T46158, T46158 9421 Lambda-PRL2 Arabidopsis thaliana cDNA clo... 36 1.8 AA520866, AA520866 TgESTzz68e05.rl TgME49 invivo Bradyzoite c... 36 1.8 Z17562, ATTS0136 A. thaliana transcribed sequence; clone TAT... 36 1.8 AA520811, AA520811 TgESTzz64d05.r1 TgME49 invivo Bradyzoite c... 36 1.8 AA567455, AA567455 HL01288.5prime HL Drosophila melanogaster ... 36 1.8 AA519228, AA519228 TgESTzz39h02.s1 TgME49 invivo Bradyzoite c... 36 1.8 AA531917, AA531917 TgESTzz48f01.r1 TgME49 invivo Bradyzoite c... AA519829, AA519829 TgESTzz36a02.r1 TgME49 invivo Bradyzoite c... 36 1.8 AA520185, AA520185 TgESTzz39d03.s1 TgME49 invivo Bradyzoite c... 36 1.8 C37095, C37095 C.elegans cDNA clone yk482c11: 3' end, singl... 36 1.8

T46009, T46009 9272 Lambda-PRL2 Arabidopsis thaliana cDNA clo... 36 1.8 T20458, T20458 2466 Lambda-PRL2 Arabidopsis thaliana cDNA clo... 36 1.8 F14402, ATTS5324 A. thaliana transcribed sequence; clone TAP... 36 1.8 T20404, T20404 2412 Lambda-PRL2 Arabidopsis thaliana cDNA clo... 36 1.8 AA274295, AA274295 TgESTzz24c11.s1 TgME49 invivo Bradyzoite c... 36 1.8 AA699152, AA699152 HL07807.5prime HL Drosophila melanogaster ... 36 1.8 AA902065, AA902065 NCM1A12T3 Mycelial Neurospora crassa cDNA ... 36 1.8

### **SEQ ID NO:558**

AF016585, AF016585 Streptomyces caelestis cytochrome P-450 hy... 42 0.092 U50719, MSU50719 Manduca sexta neuroglian mRNA, complete cds 40 0.36 Z97208, SPAC15A10 S.pombe chromosome I cosmid c15A10 40 0.36 AC003063, AC003063 Mus musculus Chromosome 16 BAC Clone b40-o... 40 0.36 X66455, MMFGFR2 M.musculus promoter region of fibroblast gro... 40 0.36 D83785, D83785 Human mRNA for KIAA0200 gene, complete cds 40 0.36 AC000398, AC000398 Genomic sequence from Mouse 11, complete s... 38 1.4 AF062345, AF062345 Caulobacter crescentus Sts1 (sts1), S-laye... 38 1.4 X12359, RCNIFR12 Rhodobacter capsulatus nifR1 and nifR2 gene X72382, RCNIFR3 R.capsulatus nifR3 DNA 38 1.4

### **HUMAN ESTs**

R36714, R36714 yh93g06.s1 Homo sapiens cDNA clone 137338 3'. 775 0.0 D61030, HUM149A04B Human fetal brain cDNA 5'-end GEN-149A04. 666 0.0 D60944, HUM141D02B Human fetal brain cDNA 5'-end GEN-141D02. 656 0.0 H03308, H03308 yj47d09.s1 Homo sapiens cDNA clone 151889 3'. 609 e-172 AA435561, AA435561 zt73d09.s1 Soares testis NHT Homo sapiens ... 587 e-166 AA977877, AA977877 oq56d03.s1 NCI\_CGAP\_Kid5 Homo sapiens cDNA... 571 e-161 AA846787, AA846787 aj41h03.s1 Soares testis NHT Homo sapiens ... 563 e-159 AA972542, AA972542 oo82e01.s1 NCI\_CGAP\_Kid5 Homo sapiens cDNA... 561 e-158 AA954270, AA954270 on72e06.s1 Soares\_NFL\_T\_GBC\_S1 Homo sapien... 557 e-157 AA740333, AA740333 ob23c02.s1 NCI\_CGAP\_Kid5 Homo sapiens cDNA... 557 e-157 AA999722, AA999722 ov04c06.sl NCI\_CGAP Kid3 Homo sapiens cDNA... 555 e-156 AA970621, AA970621 op40h08.s1 Soares\_NFL\_T\_GBC\_S1 Homo sapien... 551 e-155 AA932930, AA932930 oo04g11.s1 Soares\_NFL T\_GBC\_S1 Homo sapien... 541 e-152 AA725406, AA725406 ai13b11.s1 Soares parathyroid tumor NbHPA ... 539 e-152 W74439, W74439 zd75d10.s1 Soares fetal heart NbHH19W Homo sap... 539 e-152 AA868538, AA868538 ak43e08.s1 Soares testis NHT Homo sapiens ... 539 e-152 R79832, R79832 yi89b08.s1 Homo sapiens cDNA clone 146391 3' s... 537 e-151

R63227, R63227 yi07e06.s1 Homo sapiens cDNA clone 138562 3'. 535 e-150 AI027967, AI027967 ov84d04.x1 Soares testis NHT Homo sapiens ... 535 e-150 AA776717, AA776717 ah49d07.s1 Soares testis NHT Homo sapiens ... 535 e-150 AI040961, AI040961 ov53d06.x1 Soares testis NHT Homo sapiens ... 533 e-150 AI024835, AI024835 ov35h09.x1 Soares testis NHT Homo sapiens ... 533 e-150 AA740667, AA740667 ob01g12.s1 NCI CGAP Kid3 Homo sapiens cDNA... 531 e-149 AA994527, AA994527 ou42h06.s1 Soares NFL T GBC S1 Homo sapien... 531 e-149 AA932728, AA932728 oo31g06.s1 NCI CGAP Lu5 Homo sapiens cDNA ... 529 e-149 AI001978, AI001978 ot39f03.s1 Soares testis NHT Homo sapiens ... 529 e-149 N37092, N37092 yy41g08.s1 Homo sapiens cDNA clone 273854 3'. 529 e-149 N27547, N27547 yy01e05.s1 Homo sapiens cDNA clone 269984 3'. 527 e-148 AA883578, AA883578 al46b08.sl Soares NFL T GBC S1 Homo sapien... 527 e-148 AA890154, AA890154 al53f07.s1 Soares\_NFL T GBC S1 Homo sapien... 525 e-147 AA757222, AA757222 ah56f11.s1 Soares testis NHT Homo sapiens ... 525 e-147 AA456074, AA456074 aa17b07.s1 Soares NhHMPu S1 Homo sapiens c... 523 e-147 AA884285, AA884285 am32f04.sl Soares NFL T GBC S1 Homo sapien... 523 e-147 AA969436, AA969436 op53e12.s1 Soares\_NFL\_T\_GBC\_S1 Homo sapien... 521 e-146 AA952918, AA952918 on55h11.s1 Soares NFL T GBC S1 Homo sapien... 521 e-146 AA971938, AA971938 op88b01.s1 Soares\_NFL\_T\_GBC\_S1 Homo sapien... 521 e-146 R25112, R25112 yh36b12.s1 Homo sapiens cDNA clone 131807 3'. 519 e-146 AA865258, AA865258 og87d08.s1 NCI\_CGAP\_Kid5 Homo sapiens cDNA... 519 e-146 AA758323, AA758323 ah65e11.s1 Soares testis NHT Homo sapiens ... 519 e-146 AA972041, AA972041 op88e06.s1 Soares\_NFL\_T\_GBC\_S1 Homo sapien... 519 e-146 R76443, R76443 vi58e11.s1 Homo sapiens cDNA clone 143468 3'. AA917965, AA917965 om37e04.s1 Soares NFL T GBC S1 Homo sapien... 517 e-145 AA505880, AA505880 ni01a09.s1 NCI CGAP Br2 Homo sapiens cDNA ... 517 e-145 AA906270, AA906270 oj98e12.s1 Soares NFL T GBC S1 Homo sapien... 517 e-145 AA758549, AA758549 ah70b04.s1 Soares testis NHT Homo sapiens ... 517 e-145 AA927156, AA927156 om20f05.s1 Soares NFL T GBC S1 Homo sapien... 515 e-144 AA976254, AA976254 oo30f08.s1 NCI CGAP Lu5 Homo sapiens cDNA ... 515 e-144 R23891, R23891 yh28a12.s1 Homo sapiens cDNA clone 131038 3'. 515 e-144 AA938552, AA938552 oo78g11.s1 NCI\_CGAP\_Kid5 Homo sapiens cDNA... 513 e-144 AA483809, AA483809 ne41c08.s1 NCI\_CGAP\_Co3 Homo sapiens cDNA ... 513 e-144 AA962659, AA962659 or31f10.s1 NCI\_CGAP GC3 Homo sapiens cDNA ... 511 e-143 AA724803, AA724803 ai05f02.s1 Soares parathyroid tumor NbHPA ... 511 e-143 AA410432, AA410432 zv12c09.s1 Soares NhHMPu S1 Homo sapiens c... 511 e-143 AA775373, AA775373 ad19c07.s1 Soares NbHFB Homo sapiens cDNA ... 511 e-143 AA758038, AA758038 ah67h09.s1 Soares testis NHT Homo sapiens ... 509 e-143 AA904368, AA904368 ol15d02.s1 Soares NFL T GBC S1 Homo sapien... 509 e-143 AA861386, AA861386 ak37b11.s1 Soares testis NHT Homo sapiens ... 507 e-142 R31547, R31547 yh72g03.s1 Homo sapiens cDNA clone 135316 3'. 505 e-141 AA843421, AA843421 ak07f11.s1 Soares parathyroid tumor NbHPA ... 504 e-141 H02479, H02479 yi35e10.s1 Homo sapiens cDNA clone 150762 3'. 504 e-141 N29346, N29346 yw85c12.s1 Homo sapiens cDNA clone 259030 3'. 504 e-141 AA815351, AA815351 ai63g05.s1 Soares testis NHT Homo sapiens ... 504 e-141

AA923373, AA923373 ol46e03.s1 Soares NFL T GBC S1 Homo sapien... 502 e-140 H01218, H01218 yj31c08.s1 Homo sapiens cDNA clone 150350 3'. 500 e-140 AA988977, AA988977 or87e11.s1 NCI\_CGAP\_Lu5 Homo sapiens cDNA ... 500 e-140 AA628621, AA628621 af40c02.s1 Soares total fetus Nb2HF8 9w Ho... 500 e-140 AA442745, AA442745 zv60a07.s1 Soares testis NHT Homo sapiens ... 498 e-139 AA777492, AA777492 zj02e07.s1 Soares fetal liver spleen 1NFLS... 498 e-139 R73670, R73670 yi55f03.s1 Homo sapiens cDNA clone 143165 3'. 498 e-139 H12460, H12460 yj12d05.s1 Homo sapiens cDNA clone 148521 3'. 498 e-139 AA875917, AA875917 oj15a08.s1 NCI\_CGAP\_Kid5 Homo sapiens cDNA... 496 e-138 R76230, R76230 yi71g11.s1 Homo sapiens cDNA clone 144740 3'. 494 e-138 AA970616, AA970616 op40h03.s1 Soares\_NFL\_T\_GBC\_S1 Homo sapien... 494 e-138 AA912408, AA912408 ol23a05.s1 Soares\_NFL\_T\_GBC\_S1 Homo sapien... 492 e-137 AA910051, AA910051 ol40e08.s1 Soares\_NFL\_T\_GBC\_S1 Homo sapien... 492 e-137 AA815444, AA815444 ai65b11.s1 Soares testis NHT Homo sapiens ... 492 e-137 R76814, R76814 yi62f06.s1 Homo sapiens cDNA clone 143843 3'. 488 e-136 AA954722, AA954722 oo84c12.s1 NCI\_CGAP\_Kid5 Homo sapiens cDNA... 488 e-136 R65987, R65987 yi23e10.s1 Homo sapiens cDNA clone 140106 3'. 486 e-136 R63480, R63480 yi08e11.s1 Homo sapiens cDNA clone 138668 3'. 486 e-136 AA885425, AA885425 am12h09.s1 Soares NFL T GBC S1 Homo sapien... 486 e-136 AA884231, AA884231 am32a01.s1 Soares NFL T GBC S1 Homo sapien... 484 e-135 AA885048, AA885048 am11a12.s1 Soares NFL T GBC S1 Homo sapien... 482 e-134 AA996162, AA996162 os14f10.s1 NCI\_CGAP\_Lu5 Homo sapiens cDNA ... 482 e-134 AA748637, AA748637 ny10a02.s1 NCI\_CGAP\_GCB1 Homo sapiens cDNA... 482 e-134 AI031908, AI031908 ow47e12.x1 Soares parathyroid tumor NbHPA ... 482 e-134 AA884703, AA884703 am18e02.s1 Soares NFL T GBC S1 Homo sapien... 480 e-134 AA928243, AA928243 on87c10.s1 Soares\_NFL\_T\_GBC\_S1 Homo sapien... 480 e-134 AI025986, AI025986 ow03a09.s1 Soares\_parathyroid\_tumor\_NbHPA ... 478 e-133 AA897637, AA897637 oj72g07.s1 Soares\_NFL\_T\_GBC\_S1 Homo sapien... 472 e-131 AA877346, AA877346 01c07.s1 NCI\_CGAP\_Co10 Homo sapiens cDNA... 472 e-131 AA833569, AA833569 aj46b02.s1 Soares testis NHT Homo sapiens ... 472 e-131 AA832163, AA832163 oc91b02.s1 NCI\_CGAP\_GCB1 Homo sapiens cDNA... 470 e-131 R89052, R89052 ym99e08.s1 Homo sapiens cDNA clone 167078 3'. 470 e-131 N26589, N26589 yx91f03.s1 Homo sapiens cDNA clone 269117 3'. 460 e-128 R73883, R73883 yi56c03.s1 Homo sapiens cDNA clone 143236 3'. 454 e-126 AA579968, AA579968 ng51c03.s1 NCI\_CGAP\_Co3 Homo sapiens cDNA ... 444 e-123 AA843427, AA843427 ak07g06.s1 Soares parathyroid tumor NbHPA ... 438 e-121 AA705903, AA705903 ah42g12.s1 Soares testis NHT Homo sapiens ... 436 e-121 AA835882, AA835882 oc81d05.s1 NCI\_CGAP\_GCB1 Homo sapiens cDNA... 434 e-120 AA812583, AA812583 aj43b02.s1 Soares testis NHT Homo sapiens ... 432 e-119 AA512970, AA512970 nj16b08.s1 NCI\_CGAP\_Pr22 Homo sapiens cDNA... 432 e-119 R26664, R26664 yh35g10.s1 Homo sapiens cDNA clone 131778 3'. AA429715, AA429715 zv60a07.rl Soares testis NHT Homo sapiens ... 414 e-114 H17430, H17430 ym40f09.s1 Homo sapiens cDNA clone 50607 3'. 404 e-111 AA436117, AA436117 zu03d10.rl Soares testis NHT Homo sapiens ... 402 e-110 AA099077, AA099077 zl77a09.sl Stratagene colon (#937204) Homo... 400 e-110

R72440, R72440 yj90h02.s1 Homo sapiens cDNA clone 156051 3'. 379 e-103 AA577436, AA577436 nm96h06.s1 NCI\_CGAP\_Co9 Homo sapiens cDNA ... 351 4e-95 AA516390, AA516390 nf55e03.s1 NCI\_CGAP Co3 Homo sapiens cDNA ... 347 6e-94 AA534533, AA534533 nf80h06.s1 NCI\_CGAP\_Co3 Homo sapiens cDNA ... 341 3e-92 AA541583, AA541583 ni89f05.s1 NCI\_CGAP\_Pr21 Homo sapiens cDNA... 311 3e-83 N72191, N72191 yz99f07.s1 Homo sapiens cDNA clone 291205 3'. 303 8e-81 AA905015, AA905015 ok09b08.s1 Soares\_NFL\_T\_GBC\_S1 Homo sapien... 303 8e-81 AA393148, AA393148 zt73d09.r1 Soares testis NHT Homo sapiens ... 287 4e-76 AA939048, AA939048 op56h04.s1 Soares\_NFL\_T\_GBC\_S1 Homo sapien... 256 2e-66 AA412317, AA412317 zt97c05.r1 Soares testis NHT Homo sapiens ... 246 2e-63 R65986, R65986 yi23e10.rl Homo sapiens cDNA clone 140106 5'. 238 4e-61 AA400827, AA400827 zt76c07.s1 Soares testis NHT Homo sapiens ... 232 2e-59 W00472, W00472 yz99f07.rl Homo sapiens cDNA clone 291205 5'. AA860558, AA860558 aj81e09.s1 Soares parathyroid tumor NbHPA ... 180 8e-44 AA455577, AA455577 aa17b07.r1 Soares NhHMPu S1 Homo sapiens c... 176 1e-42 AA583931, AA583931 nn64e04.s1 NCI\_CGAP\_Lar1 Homo sapiens cDNA... 172 2e-41 AA907332, AA907332 ol22g11.s1 Soares NFL T\_GBC S1 Homo sapien... 168 3e-40 R71169, R71169 yi53a12.rl Homo sapiens cDNA clone 142942 5'. W79084, W79084 zd75d10.rl Soares fetal heart NbHH19W Homo sap... 155 4e-36 AA295914, AA295914 EST101137 Thymus III Homo sapiens cDNA 5' end 135 4e-30 AA860415, AA860415 aj60d10.s1 Soares testis NHT Homo sapiens ... 100 2e-19 H01351, H01351 yi99a07.rl Homo sapiens cDNA clone 147348 5'. 98 9e-19 AA709286, AA709286 ai21g07.s1 Soares testis NHT Homo sapiens ... 96 3e-18 AA931370, AA931370 oo03d01.s1 Soares\_NFL T GBC S1 Homo sapien... 96 3e-18 AA501911, AA501911 ng54a08.s1 NCI\_CGAP\_Li2 Homo sapiens cDNA ... 94 1e-17 AA548419, AA548419 nj14g09.s1 NCI\_CGAP\_Pr22 Homo sapiens cDNA... 92 5e-17 AA588892, AA588892 no23b06.s1 NCI\_CGAP\_Pr22 Homo sapiens cDNA... 92 5e-17 AI025228, AI025228 ov40h08.x1 Soares testis NHT Homo sapiens ... 76 3e-12 R73757, R73757 yi55f03.r1 Homo sapiens cDNA clone 143165 5'. 74 1e-11 R23710, R23710 yh35g10.rl Homo sapiens cDNA clone 131778 5'. 56 3e-06 N40362, N40362 yy01e05.rl Homo sapiens cDNA clone 269984 5'. 50 2e-04 H59895, H59895 yr04c12.rl Homo sapiens cDNA clone 204310 5'. 48 7e-04 H12509, H12509 yj12d05.rl Homo sapiens cDNA clone 148521 5'. 44 0.011 N20344, N20344 yx38d02.s1 Homo sapiens cDNA clone 264003 3'. 38 0.70 AA614692, AA614692 np52b10.s1 NCI\_CGAP\_Br1.1 Homo sapiens cDN... 38 0.70 H30707, H30707 yo78f07.rl Homo sapiens cDNA clone 184069 5'. 36 2.7 H52973, H52973 yq82e04.rl Homo sapiens cDNA clone 202302 5'. 36 2.7 AA218550, AA218550 zq96b02.r1 Stratagene NT2 neuronal precurs... 36 2.7 AA312481, AA312481 EST183215 Jurkat T-cells VI Homo sapiens c... 36 2.7 AA632009, AA632009 np74c07.s1 NCI\_CGAP\_Br2 Homo sapiens cDNA ... 36 2.7 H13363, H13363 yl71b10.r1 Homo sapiens cDNA clone 43343 5'. 36 2.7 AI022018, AI022018 ow64d01.x1 Soares senescent fibroblasts Nb... 36 2.7 AA781996, AA781996 ai75a06.s1 Soares testis NHT Homo sapiens ... 36 2.7 N21623, N21623 yx60a09.s1 Homo sapiens cDNA clone 266104 3'. 36 2.7 AA326194, AA326194 EST29340 Cerebellum II Homo sapiens cDNA 5... 36 2.7

C76071, C76071 Mus musculus 3.5-dpc blastocyst cDNA 3'-end s... 250 4e-65 AA051612, AA051612 mj52c07.r1 Soares mouse embryo NbME13.5 14... 238 1e-61 AA561635, AA561635 vl01h07.rl Knowles Solter mouse blastocyst... 234 2e-60 AA288419, AA288419 vb14h01.r1 Soares mouse NML Mus musculus c... 220 3e-56 AA212883, AA212883 mw78e10.rl Soares mouse NML Mus musculus c... 220 3e-56 AA268018, AA268018 vb08e07.r1 Soares mouse NML Mus musculus c... 212 8e-54 AA692427, AA692427 vt59b07.rl Barstead mouse irradiated colon... 200 3e-50 W18566, W18566 mb98h02.rl Soares mouse p3NMF19.5 Mus musculus... 192 7e-48 AA543948, AA543948 vj69b08.rl Knowles Solter mouse blastocyst... 147 4e-34 W41070, W41070 mc39b06.r1 Soares mouse p3NMF19.5 Mus musculus... 123 5e-27 Z31174, MMTEST52 M.musculus expressed sequence tag MTEST52 117 3e-25 AA530723, AA530723 vj32f07.r1 Stratagene mouse diaphragm (#93... 74 5e-12 AA966940, AA966940 ua38c01.rl Soares mouse mammary gland NbMM... 72 2e-11 AA111079, AA111079 mp50e01.rl Barstead MPLRB1 Mus musculus cD... 44 0.004 AA049187, AA049187 mj51a02.rl Soares mouse embryo NbME13.5 14... 36 0.99 AA058246, AA058246 mg74e12.rl Soares mouse embryo NbME13.5 14... 36 0.99 AA153730, AA153730 mq60a02.r1 Soares 2NbMT Mus musculus cDNA ... 36 0.99 AA473959, AA473959 vd02b12.s1 Knowles Solter mouse 2 cell Mus... 36 0.99 W47887, W47887 mc83h09.r1 Soares mouse embryo NbME13.5 14.5 M... 36 0.99 AA033312, AA033312 mi43g01.rl Soares mouse embryo NbME13.5 14... 36 0.99 AA980820, AA980820 ua46a04.rl Soares mouse mammary gland NbMM... 36 0.99 Z31139, MMTEST427 M.musculus expressed sequence tag MTEST427 C76637, C76637 Mus musculus 3.5-dpc blastocyst cDNA 3'-end s... 34 3.9 AI049314, AI049314 uc87b10.y1 Sugano mouse kidney mkia Mus mu... 34 3.9 AA670807, AA670807 vs70b02.rl Stratagene mouse skin (#937313)... 34 3.9 AA727571, AA727571 vv01h11.rl Stratagene mouse skin (#937313)... 34 3.9 AA571966, AA571966 vg12f07.r1 Soares mouse NbMH Mus musculus ... 34 3.9 W37059, W37059 mb73f10.r1 Soares mouse p3NMF19.5 Mus musculus... 34 3.9 AA760280, AA760280 vv74h11.rl Stratagene mouse skin (#937313)... 34 3.9 AA799036, AA799036 vn40c12.r1 Stratagene mouse skin (#937313)... 34 3.9 AA432831, AA432831 vf28g07.rl Knowles Solter mouse 8 cell Mus... 34 3.9 AA562435, AA562435 vk98c01.rl Knowles Solter mouse blastocyst... 34 3.9 AA726680, AA726680 vu93g12.rl Stratagene mouse skin (#937313)... 34 3.9 AA217464, AA217464 mu87d11.rl Soares mouse lymph node NbMLN M... 34 3.9 AA790564, AA790564 vx71e06.rl Stratagene mouse skin (#937313)... 34 3.9 AA033172, AA033172 mi37f06.rl Soares mouse embryo NbME13.5 14... 34 3.9 AA616204, AA616204 vo96h02.rl Soares mouse mammary gland NbMM... 34 3.9 AA982055, AA982055 ua37h05.rl Soares mouse mammary gland NbMM... 34 3.9 W47850, W47850 mc82h10.rl Soares mouse embryo NbME13.5 14.5 M... 34 3.9 AA537538, AA537538 vk48c12.rl Soares mouse mammary gland NbMM... 34 3.9 AA636986, AA636986 vn05f04.rl Knowles Solter mouse blastocyst... 34 3.9

AI043768, AI043768 UI-R-C0-jm-d-11-0-UI.s1 UI-R-C0 Rattus nor... 174 1e-42 AA531635, AA531635 TgESTzz29b08.r1 TgME49 invivo Bradyzoite c... 38 0.22 AA944260, AA944260 EST199759 Normalized rat embryo, Bento Soa... 38 0.22 AI008930, AI008930 EST203381 Normalized rat embryo, Bento Soa... 36 0.87 D15788, RICC1258A Rice cDNA, partial sequence (C1258A). 36 0.87 AA963741, AA963741 UI-R-C0-gt-b-09-0-UI.s1 UI-R-C0 Rattus nor... 36 0.87 AA951235, AA951235 LD31601.3prime LD Drosophila melanogaster ... 34 3.5 C20118, C20118 Rice cDNA, partial sequence (E11542\_2A) 34 3.5 AA820317, AA820317 LD23876.5prime LD Drosophila melanogaster ... 34 3.5 AA950448, AA950448 LD30237.3prime LD Drosophila melanogaster ... 34 3.5

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U83883, RNU83883 Rattus norvegicus p105 coactivator mRNA, com... 42 0.11 V00722, MMBGL1 Mouse gene for beta-1-globin. X14061, MMBGCXD M.musculus beta-globin complex DNA for y, bh... 40 0.45 U20824, EHVU20824 Equine herpesvirus 2, complete genome 38 1.8 U04106, PFU04106 Pleurotus fossulatus D1822, mating group VI.... 38 1.8 U04101, POU04101 Pleurotus ostreatus D1742, Japan, mating gro... 38 1.8 AC005174, AC005174 Homo sapiens clone UWGC:g1564a012 from 7p1... 38 1.8 M18680, HUMRGAPS Homo sapiens 5S rRNA pseudogene. AL022121, MTV025 Mycobacterium tuberculosis H37Rv complete g... 38 1.8 AF038379, AF038379 Leishmania amazonensis ribosomal protein S... 38 1.8 Z11528, THIGPMR T.harzianum mRNA for imidazoleglycerolphosphate 38 1.8 U32622, CTU32622 Comamonas testosteroni TsaR (tsaR), toluenes... 38 1.8 U04102, POU04102 Pleurotus ostreatus D1743, Japan, mating gro... 38 1.8 U04105, PFU04105 Pleurotus fossulatus D1821, mating group VI,... 38 1.8 U04109, PEU04109 Pleurotus eryngii D1832, mating group VI rib... 38 1.8 U65606, BSU65606 Basidiomycete from a bamboo (Phyllostachys p... 38 1.8

# **HUMAN ESTs**

R49969, R49969 yj56c07.s1 Homo sapiens cDNA clone 152748 3' s... 523 e-147 AA834501, AA834501 of21c02.s1 NCI\_CGAP\_Kid6 Homo sapiens cDNA... 381 e-104 W96422, W96422 ze43a05.s1 Soares retina N2b4HR Homo sapiens c... 315 2e-84 R47821, R47821 yj56c07.r1 Homo sapiens cDNA clone 152748 5'. 214 7e-54 AA761660, AA761660 nz24b09.s1 NCI\_CGAP\_GCB1 Homo sapiens cDNA... 212 3e-53 AA887861, AA887861 nq99b07.s1 NCI\_CGAP\_Co10 Homo sapiens cDNA... 74 2e-11 AA644044, AA644044 nm20b12.s1 NCI\_CGAP\_Co10 Homo sapiens cDNA... 72 6e-11

AA115963, AA115963 zm78d11.s1 Stratagene neuroepithelium (#93... 40 0.22 AA779271, AA779271 zj43f02.s1 Soares fetal liver spleen 1NFLS... 40 0.22 T65600, T65600 yc76a04.r1 Homo sapiens cDNA clone 21496 5'. 38 0.86 AA515882, AA515882 nf67f10.s1 NCI\_CGAP\_Co3 Homo sapiens cDNA ... 38 0.86 AA664812, AA664812 nu69b05.s1 NCI\_CGAP\_Alv1 Homo sapiens cDNA... 36 3.4 T83365, T83365 ye03f05.s1 Homo sapiens cDNA clone 116673 3'. 36 3.4 AA009773, AA009773 zi04d04.s1 Soares fetal liver spleen 1NFLS... 36 3.4 AA916894, AA916894 og34g10.s1 NCI\_CGAP\_Br7 Homo sapiens cDNA ... 36 3.4 N27865, N27865 yy02g03.s1 Homo sapiens cDNA clone 270100 3'. 36 3.4 AA953544, AA953544 om79g06.s1 NCI\_CGAP\_Kid3 Homo sapiens cDNA... 36 3.4 AA505576, AA505576 nh93f03.s1 NCI CGAP Br2 Homo sapiens cDNA ... 36 3.4 H30276, H30276 yp42f05.s1 Homo sapiens cDNA clone 190113 3'. 36 3.4 AA699914, AA699914 zi61f08.s1 Soares fetal liver spleen 1NFLS... 36 3.4 AA595583, AA595583 nk92c04.s1 NCI\_CGAP Col1 Homo sapiens cDNA... 36 3.4 AA351139, AA351139 EST58769 Infant brain Homo sapiens cDNA 5'... 36 3.4 AA810167, AA810167 ob88a03.s1 NCI\_CGAP\_GCB1 Homo sapiens cDNA... 36 3.4 H50257, H50257 yo28a07.rl Homo sapiens cDNA clone 179220 5'. 36 3.4 W19939, W19939 zb37e09.rl Soares parathyroid tumor NbHPA Homo... 36 3.4 R19840, R19840 yg30e11.r1 Homo sapiens cDNA clone 33837 5'. 36 3.4 AA514234, AA514234 nf56e10.s1 NCI\_CGAP\_Co3 Homo sapiens cDNA ... 36 3.4

AA183407, AA183407 ms AA821640, AA821640 vw AA289310, AA289310

AA900756, AA900756 UI-R-E0-di-d-04-0-UI.s1 UI-R-E0 Rattus nor... 46 0.001 T18416, T18416 6c02e07t7 etiolated seedling Zea mays cDNA clo... 40 0.069 AA817427, AA817427 LD22827.5prime LD Drosophila melanogaster ... 36 1.1 AA274351, AA274351 TgESTzz25c09.s1 TgME49 invivo Bradyzoite c... 36 1.1 AA391823, AA391823 LD10747.5prime LD Drosophila melanogaster ... 36 1.1 AA274275, AA274275 TgESTzz24b02.s1 TgME49 invivo Bradyzoite c... 34 4.3 R86490, R86490 RABEST068T Oryctolagus cuniculus cDNA clone pR... 34 4.3 AA965817, AA965817 o5g08a1.r1 Aspergillus nidulans 24hr asexu... 34 4.3

**SEQ ID NO:560** 

X81198, L35746, L49403, U21317, Z35640, AL010273, U09850, AF071771, Z96434,

Z50028, X72735, U13072, Z34294, AB002109, X68401, M92840, D88399, Z36238, AF000262, Z46828,

#### **HUMAN ESTs**

AA215808, AA215808 zr98b10.rl NCI\_CGAP\_GCB1 Homo sapiens cDNA... 1082 0.0 N75131, N75131 yz29g07.r1 Soares multiple sclerosis 2NbHMSP H... 989 0.0 AA709149, AA709149 zf98g05.s1 Soares fetal heart NbHH19W Homo... 985 0.0 AA428341, AA428341 zw18f09.s1 Soares ovary tumor NbHOT Homo s... 967 0.0 AA043426, AA043426 zk54h09.r1 Soares pregnant uterus NbHPU Ho... 870 0.0 AA878521, AA878521 oj19c01.s1 NCI\_CGAP\_Kid5 Homo sapiens cDNA... 844 0.0 AA599696, AA599696 ag10h01.s1 Gessler Wilms tumor Homo sapien... 842 0.0 W52304, W52304 zc47c08.rl Soares senescent fibroblasts NbHSF ... 841 0.0 AA043427, AA043427 zk54h09.s1 Soares pregnant uterus NbHPU Ho... 769 0.0 N64314, N64314 yz46a12.s1 Homo sapiens cDNA clone 286078 3'. N52360, N52360 yz29g07.s1 Soares multiple sclerosis 2NbHMSP H... 753 0.0 AA290863, AA290863 zt19a08.s1 Soares ovary tumor NbHOT Homo s... 747 0.0 AA768023, AA768023 oa60e03.s1 NCI\_CGAP GCB1 Homo sapiens cDNA... 728 0.0 AA872018, AA872018 oi05f08.s1 NCI\_CGAP\_GC4 Homo sapiens cDNA ... 718 0.0 AA164765, AA164765 zp01g09.s1 Stratagene ovarian cancer (#937... 716 0.0 AA814881, AA814881 oa75e02.s1 NCI\_CGAP\_GCB1 Homo sapiens cDNA... 708 0.0 R86915, R86915 yq30f07.r1 Homo sapiens cDNA clone 197317 5'. W56703, W56703 zd14e01.rl Soares fetal heart NbHH19W Homo sap... 642 0.0 R84872, R84872 yq27e01.r1 Soares fetal liver spleen 1NFLS Hom... 636 0.0 D79691, HUM307D10B Human aorta cDNA 5'-end GEN-307D10. 630 e-179 AA025638, AA025638 ze90d11.s1 Soares fetal heart NbHH19W Homo... 626 e-178 AA298883, AA298883 EST114512 Pancreas tumor I Homo sapiens cD... 624 e-177 R86903, R86903 yq30d07.r1 Homo sapiens cDNA clone 197293 5'. AA033584, AA033584 zk21b12.s1 Soares pregnant uterus NbHPU Ho... 618 e-175 AA633335, AA633335 nq58h09.s1 NCI\_CGAP\_Co9 Homo sapiens cDNA ... 611 e-173 AA298894, AA298894 EST114513 Pancreas tumor I Homo sapiens cD... 599 e-169 R85806, R85806 yq27e01.s1 Soares fetal liver spleen 1NFLS Hom... 595 e-168 AA872617, AA872617 oi05g07.s1 NCI\_CGAP\_GC4 Homo sapiens cDNA ... 591 e-167 H71458, H71458 yu71a06.s1 Homo sapiens cDNA clone 239218 3'. 587 e-166 AA291045, AA291045 zt19a08.rl Soares ovary tumor NbHOT Homo s... 563 e-159 H71587, H71587 yu71a06.rl Homo sapiens cDNA clone 239218 5'. 543 e-153 AA035172, AA035172 zk28g05.s1 Soares pregnant uterus NbHPU Ho... 523 e-147 AA164764, AA164764 zp01g09.r1 Stratagene ovarian cancer (#937... 517 e-145 AA297001, AA297001 EST112550 Adipose tissue, white II Homo sa... 502 e-140 AA296816, AA296816 EST112381 Aorta endothelial cells Homo sap... 500 e-139 AA769090, AA769090 oa74e12.s1 NCI CGAP GCB1 Homo sapiens cDNA... 494 e-138 H54447, H54447 yq91f04.s1 Homo sapiens cDNA clone 203167 3'. 438 e-121 H54537, H54537 yq91f04.rl Homo sapiens cDNA clone 203167 5'. 436 e-120 AI049757, AI049757 an26g03.x1 Gessler Wilms tumor Homo sapien... 430 e-119

AA033583, AA033583 zk21b12.rl Soares pregnant uterus NbHPU Ho... 422 e-116 D61748, HUM205G02B Human aorta cDNA 5'-end GEN-205G02. AA148635, AA148635 zl26d10.rl Soares pregnant uterus NbHPU Ho... 377 e-102 AA148636, AA148636 zl26d10.sl Soares pregnant uterus NbHPU Ho... 373 e-101 AA025637, AA025637 ze90d11.rl Soares fetal heart NbHH19W Homo... 371 e-101 AA932620, AA932620 oo61h04.s1 NCI\_CGAP\_Lu5 Homo sapiens cDNA ... 365 4e-99 AA385594, AA385594 EST99296 Thyroid Homo sapiens cDNA 5' end AA361957, AA361957 EST71295 T-cell lymphoma Homo sapiens cDNA... 289 2e-76 AA383998, AA383998 EST97483 Thyroid Homo sapiens cDNA 5' end ... 274 1e-71 H22175, H22175 yl38a03.rl Homo sapiens cDNA clone 160492 5'. 256 3e-66 R50060, R50060 yj59c10.rl Homo sapiens cDNA clone 153042 5'. 256 3e-66 AA229414, AA229414 nc47f12.rl NCI\_CGAP\_Pr3 Homo sapiens cDNA ... 246 3e-63 D20466, HUMGS01440 Human HL60 3'directed Mbol cDNA, HUMGS014... 208 6e-52 AA249061, AA249061 114438.seq.F Human fetal heart, Lambda ZAP... 168 5e-40 R86758, R86758 yq30f07.s1 Homo sapiens cDNA clone 197317 3'. R58025, R58025 F8018 Fetal heart Homo sapiens cDNA clone F801... 101 1e-19 AA371076, AA371076 EST82846 Prostate gland I Homo sapiens cDN... 42 0.081 AA977111, AA977111 oq24c03.s1 NCI\_CGAP\_GC4 Homo sapiens cDNA ... 40 0.32 AA608923, AA608923 af03b04.s1 Soares testis NHT Homo sapiens ... 38 1.3

gb|AA386999|AA386999 vc81b02.r1 Ko mouse embryo 11 5dpc Mus mus... 668 0.0 gb|AA589082|AA589082 vk24a08.r1 Knowles Solter mouse blastocyst... 658 0.0 gb|AA510881|AA510881 vh59c11.r1 Soares mouse mammary gland NbMM... 617 e-175 gb|AA763574|AA763574 vp07e08.r1 Soares mouse mammary gland NbMM... 615 e-174 gb|AA387423|AA387423 vc84b03.r1 Ko mouse embryo 11 5dpc Mus mus... 549 e-155 gb|AA915333|AA915333 vz28f05.r1 Soares 2NbMT Mus musculus cDNA ... 543 e-153 gb|AA816208|AA816208 vp43c10.r1 Barstead mouse irradiated colon... 444 e-123 gb|AA190043|AA190043 mt91h08.r1 Soares mouse lymph node NbMLN M... 424 e-117 gb|AA207393|AA207393 mv89c09.r1 GuayWoodford Beier mouse kidney... 394 e-108 emb|Z31258|MMTEST693 M.musculus expressed sequence tag MTEST693 gb|AA930143|AA930143 vz52d11.s1 Soares 2NbMT Mus musculus cDNA ... 293 5e-78 gb|AA170612|AA170612 ms92c09.r1 Soares mouse 3NbMS Mus musculus... 287 3e-76 gb|AA762238|AA762238 vw58h02.r1 Soares mouse mammary gland NMLM... 266 1e-69 gb|AA689028|AA689028 vs02c12.r1 Barstead mouse irradiated colon... 264 4e-69 gb|AA959938|AA959938 vw58h02.s1 Soares mouse mammary gland NMLM... 240 6e-62 dbi|D18511|MUSGS01569 Mouse 3'-directed cDNA, MUSGS01569, clon... 172 1e-41 gb|AA474393|AA474393 vd57g07.r1 Knowles Solter mouse blastocyst... 100 1e-19 gb|W97165|W97165 mf90g05.r1 Soares mouse embryo NbME13.5 14.5 M... 74 8e-12 gb|AA512077|AA512077 vj43f05.r1 Stratagene mouse skin (#937313)... 62 3e-08 gb|AA794521|AA794521 vu68e07.r1 Stratagene mouse skin (#937313)... 54 8e-06 gb|AA155454|AA155454 mn38h12.rl Beddington mouse embryonic regi... 48 5e-04 gb|W91000|W91000 mf83f06.r1 Soares mouse embryo NbME13.5 14.5 M... 40 0.12

gb|AA219917|AA219917 mv62f05.rl Soares mouse 3NME12 5 Mus muscu... 38 0.45 gb|AA529349|AA529349 vi35f08.rl Beddington mouse embryonic regi... 36 1.8 gb|AA754855|AA754855 vu51e08.rl Soares mouse mammary gland NbMM... 36 1.8

gb|AA850379|AA850379 EST193146 Normalized rat ovary, Bento Soar... 569 e-161 gb|W63375|W63375 TgESTzy68g02.r1 TgME49 Tachyzoite cDNA Toxopla... 394 e-108 gb|AA946379|AA946379 EST201878 Normalized rat lung, Bento Soare... 353 5e-96 gb|AA964427|AA964427 UI-R-E1-gp-a-08-0-UI.s1 UI-R-E1 Rattus nor... 335 1e-90 gb|AA849599|AA849599 EST192366 Normalized rat muscle, Bento Soa... 307 3e-82 gb|AA849595|AA849595 EST192362 Normalized rat muscle, Bento Soa... 307 3e-82 gb|AA850378|AA850378 EST193145 Normalized rat ovary, Bento Soar... 278 3e-73 gb|AA957389|AA957389 UI-R-E1-fu-b-04-0-UI.s1 UI-R-E1 Rattus nor... 157 6e-37 gb|AI012981|AI012981 EST207432 Normalized rat spleen, Bento Soa... 147 6e-34 dbj|C48357|C48357 C.elegans cDNA clone yk469b2 : 5' end, single... 40 0.10 gb|AA440444|AA440444 LD15290.5prime LD Drosophila melanogaster ... 36 1.6 dbj|C22690|C22690 Rice cDNA, partial sequence (S5274 4A) 36 1.6 gb|AA697626|AA697626 HL02895.5prime HL Drosophila melanogaster ... 36 1.6 gb|AA550136|AA550136 1244m3 gmbPfHB3.1, G. Roman Reddy Plasmodi... 36 1.6 gb|T43579|T43579 6842 Lambda-PRL2 Arabidopsis thaliana cDNA clo... 36 1.6 gb|AI030501|AI030501 UI-R-C0-jc-g-02-0-UI.s1 UI-R-C0 Rattus nor... 36 1.6 gb|AA056876|AA056876 SWMFCA987SK Brugia malayi microfilaria cDN... 36 1.6 gb|AA440689|AA440689 LD15550.5prime LD Drosophila melanogaster ... 36 1.6

# SEQ ID NO:561

emb|Z47552|HSFMO3 H.sapiens mRNA for flavin-containing monooxyg... 44 0.10 gb|U39966|HSFMO3G7 Homo sapiens flavin containing monooxygenase... 44 0.10 emb|AL021026|HS127D3 Homo sapiens DNA sequence from PAC 127D3 o... 44 0.10 gb|U35007|CPU35007 Carcharhinus plumbeus Ig lambda light chain ... 44 0.10 gb|U35008|CPU35008 Carcharhinus plumbeus Ig lambda light chain ... 44 0.10 dbj|D85068|RICT3A Rice transposable element T3 gene and ret... 42 0.40 dbj|D63711|RICT3 Rice transposon T3 DNA, complete sequence 42 0.40 gb|U01657|U01657 Carcharhinus plumbeus Ig lambda-chain gene, co... 42 0.40 emb|Z92540|HS179I15A Human DNA sequence from PAC 179I15, BRCA2 ... 40 1.6 dbj|AB001569|AB001569 Carrot DNA for transposon Tdc1 40 1.6 emb|X07985|DMCUT Drosophila cut locus mRNA for homeodomain-cont... 40 1.6 gb|AC005217|AC005217 Homo sapiens chromosome 5, P1 clone 1047D6... 40 1.6

### **HUMAN ESTs**

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gb|AA401219|AA401219 zv63a03.r1 Soares total fetus Nb2HF8 9w Ho... 993 0.0
gb|H69371|H69371 yu19h09.rl Homo sapiens cDNA clone 234305 5' s... 44 0.049
gb|N62576|N62576 za13d10.s1 Homo sapiens cDNA clone 292435 3' s... 42 0.19
gb|W77763|W77763 zd69c06.rl Soares fetal heart NbHH19W Homo sap... 40 0.77
gb|R14832|R14832 yf93g05.r1 Homo sapiens cDNA clone 30203 5'.
                                                                 40 0.77
gb|T90524|T90524 yd40a04.s1 Homo sapiens cDNA clone 110670 3' s... 38 3.0
gb|R91887|R91887 yq04c09.r1 Homo sapiens cDNA clone 195952 5'.
                                                                  38 3.0
gb|AA586935|AA586935 nn68h03.s1 NCI_CGAP_Lar1 Homo sapiens cDNA... 38 3.0
gb|T46987|T46987 yb12a07.s1 Homo sapiens cDNA clone 70932 3' co...
gb|AA853975|AA853975 aj51f09.s1 Soares testis NHT Homo sapiens ... 38 3.0
gb|T97059|T97059 ye50e01.rl Homo sapiens cDNA clone 121176 5'.
                                                                 38 3.0
gb|AA883119|AA883119 am15h02.s1 Soares NFL T GBC S1 Homo sapien... 38 3.0
gb|AA860074|AA860074 ak45b06.s1 Soares testis NHT Homo sapiens ... 38 3.0
gb|AA889618|AA889618 ak28f06.s1 Soares testis NHT Homo sapiens ... 38 3.0
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gb|AA230450|AA230450 mv73c06.r1 Soares mouse 3NME12 5 Mus muscu... 38 1.1 gb|AA058041|AA058041 mj58e08.r1 Soares mouse embryo NbME13.5 14... 38 1.1 gb|AA152953|AA152953 mq54a03.r1 Soares 2NbMT Mus musculus cDNA ... 38 1.1 gb|W34414|W34414 ma98b07.r1 Soares mouse p3NMF19.5 Mus musculus... 38 1.1 gb|AA465969|AA465969 ve90c06.s1 Knowles Solter mouse 2 cell Mus... 38 1.1 gb|AA261173|AA261173 mz62b11.r1 Soares mouse lymph node NbMLN M... 38 1.1 gb|AA238109|AA238109 mw97b05.r1 Soares mouse NML Mus musculus c... 38 1.1 dbi|C86549|C86549 Mus musculus fertilized egg cDNA 3'-end seque... 38 1.1 gb|AI048677|AI048677 ub29g09.r1 Soares 2NbMT Mus musculus cDNA ... 38 1.1 dbj|D77921|MUSC1A08 Mouse embryonal carcinoma F9 cell cDNA, C1A08 gb|AA396183|AA396183 vb45e04.r1 Soares mouse lymph node NbMLN M... 38 1.1 gb|AA465898|AA465898 vc62f12.s1 Knowles Solter mouse 2 cell Mus... 36 4.3 gb|AA041869|AA041869 mj05b12.r1 Soares mouse embryo NbME13.5 14... 36 4.3 gb|AA637824|AA637824 vr21f11.r1 Barstead mouse myotubes MPLRB5 ... 36 4.3 gb|W82563|W82563 mf05g06.r1 Soares mouse p3NMF19.5 Mus musculus... 36 4.3 gb|AA389972|AA389972 vb30e03.r1 Soares mouse lymph node NbMLN M... 36 4.3 gb|AA396253|AA396253 vb45f08.r1 Soares mouse lymph node NbMLN M... 36 4.3 gb|AA920907|AA920907 vy84f04.r1 Stratagene mouse macrophage (#9... 36 4.3 gb|AA517166|AA517166 vh98h05.r1 Barstead mouse myotubes MPLRB5 ... 36 4.3 gb|AA433599|AA433599 vf47a05.r1 Soares mouse NbMH Mus musculus ... 36 4.3 gb|AA867252|AA867252 vx25c01.r1 Soares 2NbMT Mus musculus cDNA ... 36 4.3 dbi|C85619|C85619 Mus musculus fertilized egg cDNA 3'-end seque... 36 4.3 gb|AA260277|AA260277 va93g05.r1 Soares mouse 3NME12 5 Mus muscu... 36 4.3 gb|AA172548|AA172548 mt04g11.r1 Soares mouse 3NbMS Mus musculus... 36 4.3 gb|AA266879|AA266879 mz96a02.r1 Soares mouse lymph node NbMLN M... 36 4.3 gb|AA473019|AA473019 vd43e06.r1 Barstead MPLRB1 Mus musculus cD... 36 4.3

gb|R47549|R47549 SW3ICA119SK Brugia malayi infective larva cDNA... 40 0.24 gb|H32651|H32651 EST107947 Rat PC-12 cells, untreated Rattus sp... 38 0.96 gb|AA955987|AA955987 UI-R-E1-fb-f-06-0-UI.s1 UI-R-E1 Rattus nor... 38 0.96 gb|AA819638|AA819638 UI-R-A0-an-f-03-0-UI.s1 UI-R-A0 Rattus nor... 38 0.96 gb|AI010914|AI010914 EST205365 Normalized rat muscle, Bento Soa... 38 0.96 gb|AA893199|AA893199 EST197002 Normalized rat kidney, Bento Soa... 38 0.96 gb|AA945176|AA945176 EST200675 Normalized rat liver, Bento Soar... 38 0.96 gb|R95272|R95272 SWOvL3CA167SK Onchocerca volvulus infective la... 36 3.8 gb|AA917208|AA917208 ka05f02.s1 Onchocerca volvulus infective l... 36 3.8 dbj|C62023|C62023 C.elegans cDNA clone yk249d5 : 5' end, single... 36 3.8 gb|AI013322|AI013322 EST207997 Normalized rat spleen, Bento Soa... 36 3.8 gb|AI043280|AI043280 TENU0920 T. cruzi epimastigote normalized ... 36 3.8 gb|AI009422|AI009422 EST203873 Normalized rat heart, Bento Soar... 36 3.8 gb|AI012655|AI012655 EST207106 Normalized rat placenta, Bento S... 36 3.8 dbj|C62878|C62878 C.elegans cDNA clone yk296d4: 5' end, single... 36 3.8 gb|AA915818|AA915818 SWOvL3CA1269SK Onchocerca volvulus infecti... 36 3.8 gb|W00009|W00009 TgESTzy75b07.r1 TgRH Tachyzoite cDNA Toxoplasm... 36 3.8 gb|AA943503|AA943503 EST199002 Normalized rat brain, Bento Soar... 36 3.8 gb|AA956933|AA956933 UI-R-E1-f1-b-08-0-UI.s1 UI-R-E1 Rattus nor... 36 3.8 gb|H54977|H54977 HHU16a Sorghum bicolor cv. TX430 Sorghum bicol... 36 3.8

# SEQ ID NO:562

gb|AC000112|HSAC000112 Human PAC clone DJ149P21, complete seque... 44 0.082 gb|U50197|CELF25E2 Caenorhabditis elegans cosmid F25E2. 44 0.082 dbj|AB007727|AB007727 Arabidopsis thaliana genomic DNA, chromos... 44 0.082 gb|U02562|BSU02562 Bacillus subtilis N-acetylglucosaminidase (l... 42 0.32 dbj|D45048|BACORFX Bacillus subtilis gene for beta-N-acetylgluc... 42 0.32 emb|Z70683|CEF13B12 Caenorhabditis elegans cosmid F13B12, compl... 40 1.3 emb|AL023828|CEY17G7B Caenorhabditis elegans cosmid Y17G7B, com... 40 1.3 gb|U39740|CELZC64 Caenorhabditis elegans cosmid ZC64. 40 1.3 gb|AF006490|AF006490 Gossypium hirsutum adenine nucleotide tran... 40 1.3 emb|AL010170|PFSC03098 Plasmodium falciparum DNA \*\*\* SEQUENCING... 40 1.3 gb|U53701|GHU53701 Gossypium hirsutum alcohol dehydrogenase 2d ... 40 1.3

#### **HUMAN ESTs**

gb|AA670455|AA670455 ae62h05.s1 Stratagene lung carcinoma 93721... 852 0.0 gb|AA251062|AA251062 zs07c10.r1 NCI\_CGAP\_GCB1 Homo sapiens cDNA... 795 0.0

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gb|AA669916|AA669916 ag42h08.s1 Jia bone marrow stroma Homo sap... 638 0.0
gb|AA300058|AA300058 EST12665 Uterus tumor I Homo sapiens cDNA ... 587 e-165
gb|AA664277|AA664277 ac08c05.s1 Stratagene HeLa cell s3 937216 ... 549 e-154
gb|AA373224|AA373224 EST85230 HSC172 cells I Homo sapiens cDNA ... 529 e-148
gb|AA225705|AA225705 nc10b05.rl NCI_CGAP_Prl Homo sapiens cDNA ... 515 e-144
gb|W27883|W27883 39b10 Human retina cDNA randomly primed sublib... 484 e-134
gb|R24643|R24643 yh36g05.r1 Homo sapiens cDNA clone 131864 5'.
                                                                 438 e-121
gb|N93137|N93137 zb28h06.s1 Homo sapiens cDNA clone 304955 3'.
                                                                 432 e-119
gb|AA250933|AA250933 zs07d01.s1 NCI_CGAP_GCB1 Homo sapiens cDNA... 426
gb|AA216370|AA216370 nc10b05.s1 NCI_CGAP_Pr1 Homo sapiens cDNA ... 398 e-109
gb|H26939|H26939 yl64g01.rl Homo sapiens cDNA clone 163056 5'.
                                                                394 e-108
gb|H30169|H30169 yo58g09.rl Homo sapiens cDNA clone 182176 5'.
                                                                 394 e-108
gb|W38854|W38854 zb28h06.rl Soares parathyroid tumor NbHPA Homo... 359 5e-97
gb|AA602297|AA602297 np25a11.s1 NCI_CGAP_Pr22 Homo sapiens cDNA... 281 1e-73
gb|AA167151|AA167151 zp06e09.r1 Stratagene ovarian cancer (#937... 256 6e-66
gb|AA172387|AA172387 zo99d03.s1 Stratagene ovarian cancer (#937... 234 2e-59
gb|AA173748|AA173748 zo99d03.r1 Stratagene ovarian cancer (#937... 224 2e-56
gb|T83979|T83979 yd66a11.s1 Homo sapiens cDNA clone 113180 3'.
                                                                220 3e-55
dbi|D61540|HUM415A08B Human fetal brain cDNA 5'-end GEN-415A08.
                                                                    194 2e-47
gb|N45148|N45148 yv25a05.r1 Homo sapiens cDNA clone 243728 5'.
                                                                165 2e-38
gb|AA642960|AA642960 60f07.s1 NCI_CGAP_Lym3 Homo sapiens cDNA... 147 4e-33
gb|R90980|R90980 yp93a03.r1 Homo sapiens cDNA clone 194956 5' s... 40 0.62
gb|AA521500|AA521500 aa73h08.s1 NCI_CGAP_GCB1 Homo sapiens cDNA... 40 0.62
gb|H82921|H82921 yq46h10.s1 Homo sapiens cDNA clone 198883 3' s... 40 0.62
gb|AA294871|AA294871 EST100023 Pancreas tumor I Homo sapiens cD...
dbj|D63191|HUM503F11B Human placenta cDNA 5'-end GEN-503F11.
                                                                    38 2.4
gb|AA211096|AA211096 zq89g01.s1 Stratagene hNT neuron (#937233)... 38 2.4
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gb|AA840137|AA840137 ud01e08.r1 Soares mouse uterus NMPu Mus mu... 383 e-104 gb|AA145994|AA145994 mr13h04.r1 Soares mouse 3NbMS Mus musculus... 345 3e-93 gb|AA146365|AA146365 mr05d05.r1 Soares mouse 3NbMS Mus musculus... 236 2e-60 gb|AA203902|AA203902 mu60f02.r1 Soares mouse lymph node NbMLN M... 236 2e-60 gb|AA204516|AA204516 mu66c10.r1 Soares mouse lymph node NbMLN M... 182 2e-44 gb|AA137343|AA137343 mq80g08.r1 Stratagene mouse melanoma (#937... 52 6e-05 gb|AA174717|AA174717 ms67a01.r1 Soares mouse 3NbMS Mus musculus... 48 0.001 gb|W34073|W34073 ma85d10.r1 Soares mouse p3NMF19.5 Mus musculus... 48 0.001 gb|AA289493|AA289493 vb36b01.r1 Soares mouse lymph node NbMLN M... 48 0.001 gb|AA177700|AA177700 mt33e12.r1 Soares mouse 3NbMS Mus musculus... 48 0.001 gb|AA146021|AA146021 mr13e03.r1 Soares mouse 3NbMS Mus musculus... 48 0.001 gb|AA155352|AA155352 mn43d09.r1 Beddington mouse embryonic regi... 46 0.004 gb|AA880874|AA880874 vx33b02.r1 Stratagene mouse lung 937302 Mu... 42 0.056

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gb|AA590520|AA590520 vi54b08.rl Beddington mouse embryonic regi... 38 0.88
gb|AA596629|AA596629 vm56e06.r1 Stratagene mouse Tcell 937311 M... 38 0.88
dbi|D76657|MUS75H09 Mouse embryonal carcinoma F9 cell cDNA, 75H09
                                                                     38 0.88
gb|AA050336|AA050336 mj12f05.rl Soares mouse embryo NbME13.5 14... 38 0.88
gb|AA120196|AA120196 mn35a12.r1 Beddington mouse embryonic regi... 38 0.88
gb|W85267|W85267 mf42c06.r1 Soares mouse embryo NbME13.5 14.5 M... 36 3.5
gb|AA239372|AA239372 my38f03.r1 Barstead mouse pooled organs MP... 36 3.5
gb|AA497891|AA497891 vi73c07.r1 Stratagene mouse testis (#93730... 36 3.5
gb|AA673053|AA673053 vn45e05.rl Barstead mouse myotubes MPLRB5 ... 36 3.5
emb|Z36324|MM224 M.musculus mRNA (clone 224) for expressed sequ... 36 3.5
gb|AI021128|AI021128 ub01f06.rl Soares mouse mammary gland NbMM...
gb|AA403424|AA403424 mz56f07.r1 Barstead mouse pooled organs MP... 36 3.5
gb|W66683|W66683 me23g11.rl Soares mouse embryo NbME13.5 14.5 M... 36 3.5
gb|AA689022|AA689022 vs02c03.r1 Barstead mouse irradiated colon... 36 3.5
gb|AA574590|AA574590 vn63h11.rl Barstead mouse proximal colon M... 36 3.5
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dbj|C90696|C90696 Dictyostelium discoideum slug cDNA, clone SSJ634 38 0.78 gb|AA269052|AA269052 MA1MA052.AA3 S. mansoni adult Lambda Zap S... 38 0.78 gb|AA998786|AA998786 UI-R-C0-im-e-11-0-UI.s1 UI-R-C0 Rattus nor... 38 0.78 gb|H33464|H33464 EST109494 Rat PC-12 cells, NGF-treated (9 days... 38 0.78 gb|AA390721|AA390721 LD09459.5prime LD Drosophila melanogaster ... 36 3.1 dbj|C83908|C83908 Dictyostelium discoideum slug cDNA, clone SSA567 36 3.1 gb|AA202425|AA202425 LD02606.5prime LD Drosophila melanogaster ... 36 3.1 gb|AI030951|AI030951 UI-R-C0-jf-d-04-0-UI.s1 UI-R-C0 Rattus nor... 36 3.1 gb|AA246875|AA246875 LD05855.5prime LD Drosophila melanogaster ... 36 3.1 gb|AA246875|AA246875 LD05855.5prime LD Drosophila melanogaster ... 36 3.1 gb|AA803682|AA803682 GM13955.5prime GM Drosophila melanogaster ... 36 3.1 gb|AA997528|AA997528 UI-R-C0-hw-h-11-0-UI.s1 UI-R-C0 Rattus nor... 36 3.1 gb|AA695197|AA695197 GM02389.5prime GM Drosophila melanogaster ... 36 3.1 gb|AA695197|AA695197 GM02389.5prime GM Drosophila melanogaster ... 36 3.1 gb|AA695197|AA695197 GM02389.5prime GM Drosophila melanogaster ... 36 3.1 gb|AA567339|AA567339 HL01077.5prime HL Drosophila melanogaster ... 36 3.1 gb|AA950648|AA950648 LD30547.5prime LD Drosophila melanogaster ... 36 3.1

**SEQ ID NO:563** 

#### substantially identical to D86956

SEQ ID NO:564

gb|AC004505|AC004505 Homo sapiens chromosome 20, P1 clone 86C1 ... 176 1e-41 gb|S78798|S78798 1-phosphatidylinositol-4-phosphate 5-kinase is... 115 4e-23 gb|U48696|HSU48696 Human mariner-like element-containing mRNA, ... 115 4e-23 gb|U66300|LEU66300 Lycopersicon esculentum heat shock protein (... 115 4e-23 gb|AF045432|AF045432 Danio rerio stem cell leukemia protein (ta... 111 6e-22 emb|Z97178|BVRNAEF2 Beta vulgaris cDNA for elongation factor 2 107 9e-21 gb|U39066|MMU39066 Murine MAP kinase kinase 6c mRNA, complete cds. 101 6e-19 gb|U37573|XXU37573 Shuttle expression vector pBKCMV. 96 4e-17 gb|AF033097|AF033097 Avena sativa nonphototropic hypocotyl 1 (N... 90 2e-15 gb|AF027174|AF027174 Arabidopsis thaliana cellulose synthase ca... 86 3e-14 gb|U65376|CFU65376 Canis familiaris rod photoreceptor transduci... 84 1e-13 gb|AF033565|AF033565 Mus musculus cdc2/CDC28-like protein kinas... 82 5e-13 emb|Z49980|HS2AMCP H.sapiens mRNA for ets-like protein (clone 7... 82 5e-13 emb|AJ001103|LLARCAB Lactococcus lactis arcA and arcB genes 80 2e-12 gb|U52868|CFU52868 Canis familiaris retinal cyclic-GMP phosphod... 80 2e-12 gb|G29058|G29058 chicken STS ADL368 76 3e-11 gb|G29060|G29060 chicken STS ADL352 76 3e-11 gb|U34048|HDU34048 Haemophilus ducreyi hemoglobin-binding prote... 76 3e-11 gb|U44386|SLU44386 Solanum lycopersicum heat shock protein (TFH... 68 8e-09 gb|S83098|S83098 ribosomal protein S3 [Ambystoma mexicanum=Mexi... 66 3e-08 gb|U48697|HSU48697 Human mariner-like element-containing mRNA, ... 60 2e-06 gb|AF033096|AF033096 Avena sativa nonphototropic hypocotyl 1 (N... 60 2e-06 emb|X99051|LLATTMSAT L.lagopus ATT microsatellite, locus LLST1 58 8e-06 gb|U41811|HAU41811 Homarus americanus beta-I tubulin mRNA, comp... 46 0.029 emb|X99055|LLCAMSAT1 L.lagopus CA microsatellite, locus LLSD5 44 0.12 emb|X65215|BTMISATN B.taurus microsatellite DNA (624bp) 44 0.12 gb|AE001023|AE001023 Archaeoglobus fulgidus section 84 of 172 o... 42 0.46 emb|X80164|HSPDCM4 H.salinarium phage dcm4 Virus DNA 42 0.46 emb|X87859|MTCMAJ12S C.major mitochondrial gene for 12S ribosom... 42 0.46 emb|X87861|MTCPAL12S C.pallidus mitochondrial gene for 12S ribo... 42 0.46 gb|L13767|STMSEC101A Streptomyus lividans sec101 gene, 5' end p... 42 0.46 emb|Y08962|OSTRAMBPR O.sativa mRNA for transmembrane protein >g... 40 1.8 gb|S65686|S65686 {multiple cloning sites, vector} [bacteriophag... 40 1.8 gb|J02871|HUMCP45IV Human lung cytochrome P450 (IV subfamily) B... 40 1.8 dbj|D10450|HUMRTVE Human genomic DNA, retrovirus-like element 40 1.8 gb|S65683|S65683 {multiple cloning sites, vector} [bacteriophag... 40 1.8 gb|L14950|PIGALDRED Sus scrofa aldose reductase mRNA, complete ... gb|S65693|S65693 {multiple cloning sites, vector} [bacteriophag... 40 1.8 gb|S65694|S65694 {multiple cloning sites, vector} [bacteriophag... 40 1.8 emb|AJ223292|SPAJ3292 Streptococcus pyogenes SOD gene, complete... gb|U25846|HAU25846 Homarus americanus clone LOB5 farnesoic acid... 40 1.8 emb|X16699|HSP450P2 Human mRNA for cytochrome P-450HP 40 1.8 gb|U37100|HSU37100 Homo sapiens aldose reductase-like peptide m... 40 1.8

#### **HUMAN ESTs**

gb|AA305996|AA305996 EST177003 Jurkat T-cells VI Homo sapiens c... 942 0.0 gb|AA975279|AA975279 oq36e08.s1 NCI\_CGAP\_GC4 Homo sapiens cDNA ... 900 0.0 gb|AA426359|AA426359 zw11b02.rl Soares NhHMPu S1 Homo sapiens c... 868 0.0 gb|AA424296|AA424296 zv90b08.r1 Soares NhHMPu S1 Homo sapiens c... 749 0.0 gb|AA632259|AA632259 np67d04.s1 NCI\_CGAP\_Br2 Homo sapiens cDNA ... 730 0.0 gb|H80377|H80377 yu59e01.rl Homo sapiens cDNA clone 230424 5'. gb|AA515175|AA515175 ng68f10.s1 NCI\_CGAP\_Lip2 Homo sapiens cDNA... 615 e-174 gb|AA351770|AA351770 EST59616 Infant brain Homo sapiens cDNA 5'... 611 e-172 gb|AA426522|AA426522 zw11b02.s1 Soares NhHMPu S1 Homo sapiens c... 587 e-165 gb|AA676220|AA676220 zi22a12.s1 Soares fetal liver spleen 1NFLS... 585 e-165 gb|R35132|R35132 yg60e09.r1 Homo sapiens cDNA clone 36874 5'. 579 e-163 gb|H80280|H80280 yu59e01.s1 Homo sapiens cDNA clone 230424 3'. 579 e-163 gb|H81145|H81145 yu60e01.rl Homo sapiens cDNA clone 230520 5'. 561 e-157 gb|AA311105|AA311105 EST18187 Heart I Homo sapiens cDNA 5' end 533 e-149 gb|AA380530|AA380530 EST93691 Supt cells Homo sapiens cDNA 5' end 527 e-147 gb|H81050|H81050 yu60e01.s1 Homo sapiens cDNA clone 230520 3'. 500 e-139 gb|AA460005|AA460005 zx49g07.s1 Soares testis NHT Homo sapiens ... 482 e-134 gb|AA076450|AA076450 zm91d12.r1 Stratagene ovarian cancer (#937... 466 e-129 gb|N43873|N43873 yy43e09.r1 Homo sapiens cDNA clone 274024 5'. 452 e-125 gb|AA076451|AA076451 zm91d12.s1 Stratagene ovarian cancer (#937... 418 e-115 gb|AA907095|AA907095 ol03b12.s1 NCI\_CGAP\_Lu5 Homo sapiens cDNA ... 414 e-113 gb|W01027|W01027 za56g07.rl Soares fetal liver spleen 1NFLS Hom... 262 le-67 gb|AA127183|AA127183 zn29d11.r1 Stratagene neuroepithelium NT2R... 222 1e-55 gb|H65491|H65491 yr56a08.s1 Homo sapiens cDNA clone 209270 3'. 222 1e-55 gb|N48543|N48543 yy49d08.r1 Homo sapiens cDNA clone 276879 5'. 210 4e-52 gb|R32579|R32579 yh54h06.rl Homo sapiens cDNA clone 133595 5'. 194 2e-47 gb|AA247827|AA247827 j0778.seq.F Human fetal heart, Lambda ZAP ... 117 5e-24 N84048, (many others similar, but smaller)

gb|AA589598|AA589598 vl49d08.s1 Stratagene mouse skin (#937313)... 398 e-109 gb|AA647465|AA647465 vq82f02.s1 Knowles Solter mouse 2 cell Mus... 385 e-105 gb|AA510284|AA510284 vh58f02.r1 Soares mouse mammary gland NbMM... 345 4e-93 gb|AA028696|AA028696 mi12e12.r1 Soares mouse p3NMF19.5 Mus musc... 307 9e-82 gb|N28081|N28081 MDB1409R Mouse brain, Stratagene Mus musculus ... 244 1e-62 gb|AA177452|AA177452 mt24c12.r1 Soares mouse 3NbMS Mus musculus ... 226 3e-57 gb|N28080|N28080 MDB1409 Mouse brain, Stratagene Mus musculus c... 226 3e-57 dbj|C88310|C88310 Mus musculus fertilized egg cDNA 3'-end seque... 226 3e-57 gb|AA763786|AA763786 vo99g12.r1 Soares mouse mammary gland NbMM... 94 2e-17 gb|AA667535|AA667535 vv1°b12.r1 Stratagene mouse heart (#937316... 40 0.31 gb|AA208274|AA208274 mv96a01.r1 GuayWoodford Beier mouse kidney... 38 1.2

gb|AA444814|AA444814 vg50e04.r1 Soares mouse mammary gland NbMM... 38 1.2 gb|AA763341|AA763341 vw53b12.r1 Soares mouse mammary gland NMLM... 38 1.2 gb|AA110827|AA110827 mp57a12.r1 Soares 2NbMT Mus musculus cDNA ... 38 1.2 gb|AA691932|AA691932 vt06b04.r1 Barstead mouse myotubes MPLRB5 ... 38 1.2 gb|W77233|W77233 me61f11.r1 Soares mouse embryo NbME13.5 14.5 M... 38 1.2 gb|AA072872|AA072872 mm80g08.r1 Stratagene mouse embryonic carc... 38 1.2 gb|AA980630|AA980630 ua43f05.r1 Soares mouse mammary gland NbMM... 36 4.9 gb|AA065522|AA065522 ml54d09.r1 Stratagene mouse testis (#93730... 36 4.9 gb|AA982398|AA982398 uh07b08.r1 Soares mouse hypothalamus NMHy ... 36 4.9 gb|W62610|W62610 md58c06.r1 Soares mouse embryo NbME13.5 14.5 M... 36 4.9 gb|AA286651|AA286651 vb79b02.r1 Soares mouse 3NME12 5 Mus muscu... 36 4.9 gb|AA399772|AA399772 vd70g05.r1 Beddington mouse embryonic regi... 36 4.9 gb|AA510475|AA510475 vg32h08.rl Soares mouse mammary gland NbMM... 36 4.9 gb|AA109064|AA109064 ml63g02.r1 Stratagene mouse testis (#93730... 36 4.9 gb|AA033485|AA033485 mi42c08.r1 Soares mouse embryo NbME13.5 14... 36 4.9 gb|W57221|W57221 md59g10.rl Soares mouse embryo NbME13.5 14.5 M... 36 4.9 gb|AA467106|AA467106 vd98b04.r1 Soares mouse NbMH Mus musculus ... 36 4.9 gb|W97470|W97470 mf95a11.rl Soares mouse embryo NbME13.5 14.5 M... 36 4.9 gb|AA606917|AA606917 vm91c05.rl Knowles Solter mouse blastocyst... 36 4.9 dbj|C78330|C78330 Mus musculus 3.5-dpc blastocyst cDNA 3'-end s... 36 4.9 gb|AA013753|AA013753 mh26h12.r1 Soares mouse placenta 4NbMP13.5... 36 4.9 gb|AA145240|AA145240 mr12a03.r1 Soares mouse 3NbMS Mus musculus... 36 4.9 gb|AA245533|AA245533 mx03c11.r1 Soares mouse NML Mus musculus c... 36 4.9 gb|AA770893|AA770893 vt13a08.rl Barstead mouse myotubes MPLRB5 ... 36 4.9 dbj|C79987|C79987 Mus musculus 3.5-dpc blastocyst cDNA 3'-end s... 36 4.9 gb|AA014027|AA014027 mh24a12.r1 Soares mouse placenta 4NbMP13.5... 36 4.9 dbi|C89051|C89051 Mus musculus early blastocyst cDNA, clone 01B... 36 4.9 gb|AA058308|AA058308 mj59e09.r1 Soares mouse embryo NbME13.5 14... gb|AA673826|AA673826 vu08h10.r1 Barstead mouse myotubes MPLRB5 ... 36 4.9 gb|AA637080|AA637080 vn07h04.r1 Knowles Solter mouse blastocyst... 36 4.9 gb|W44292|W44292 mc80c07.r1 Soares mouse embryo NbME13.5 14.5 M... 36 4.9

gb|AA955972|AA955972 UI-R-E1-ff-d-10-0-UI.s1 UI-R-E1 Rattus nor... 159 4e-37 gb|AA957275|AA957275 UI-R-E1-fq-f-08-0-UI.s1 UI-R-E1 Rattus nor... 157 2e-36 emb|Z84031|SSZ84031 S.scrofa mRNA; expressed sequence tag (5'; ... 111 9e-23 gb|AF041408|AF041408 Fragaria x ananassa clone FA110b 96 5e-18 gb|AA933116|AA933116 SWBmL3SA048T3 Brugia malayi L3 subtracted ... 58 1e-06 gb|AA933363|AA933363 SWBmL3SA615T3 Brugia malayi L3 subtracted ... 52 7e-05 gb|AA660164|AA660164 00001 MtRHE Medicago truncatula cDNA 5' si... 50 3e-04 gb|N37420|N37420 18647 Lambda-PRL2 Arabidopsis thaliana cDNA cl... 44 0.018 gb|H35981|H35981 14503 Lambda-PRL2 Arabidopsis thaliana cDNA cl... 44 0.018 gb|AA882627|AA882627 TENS0198 T. cruzi epimastigote normalized ... 42 0.070 gb|AA946369|AA946369 EST201868 Normalized rat lung, Bento Soare... 42 0.070

gb|AI010371|AI010371 EST204822 Normalized rat lung, Bento Soare... 42 0.070 gb|AI010257|AI010257 EST204708 Normalized rat lung, Bento Soare... 42 0.070 dbi|D39318|RICR3325A Rice cDNA, partial sequence (R3325\_1A). 40 0.28 gb|U40140|OSU40140 Oryza sativa clone pFDRRC22 mRNA sequence. 40 0.28 gb|AI009132|AI009132 EST203583 Normalized rat embryo, Bento Soa... 40 0.28 dbj|D47291|RICS12574A Rice cDNA, partial sequence (S12574 1A). 40 0.28 dbj|D47316|RICS12613A Rice cDNA, partial sequence (S12613 1A). 40 0.28 gb|T42265|T42265 5528 Lambda-PRL2 Arabidopsis thaliana cDNA clo... 40 0.28 dbj|D47631|RICS13239A Rice cDNA, partial sequence (S13239\_1A). 40 0.28 gb|AI013513|AI013513 EST208188 Normalized rat spleen, Bento Soa... 40 0.28 gb|AA751980|AA751980 96AS0896 Rice Immature Seed Lambda ZAPII c... 40 0.28 gb|AA660165|AA660165 00002 MtRHE Medicago truncatula cDNA 5' si... 40 0.28 emb|Z34868|ATTS3597 A. thaliana transcribed sequence; clone FAF... 40 0.28 dbj|D39131|RICR2302A Rice cDNA, partial sequence (R2302 1A). 40 0.28 gb|AA963968|AA963968 UI-R-C0-gs-b-05-0-UI.s1 UI-R-C0 Rattus nor... 40 0.28 gb|AA866346|AA866346 UI-R-A0-bm-a-05-0-UI.s1 UI-R-A0 Rattus nor... 40 0.28 gb|AI044437|AI044437 UI-R-C1-js-e-06-0-UI.s1 UI-R-C1 Rattus nor... 40 0.28 dbj|D41811|RICS4634A Rice cDNA, partial sequence (S4634 1A). 40 0.28 dbj|C19261|C19261 Rice cDNA, partial sequence (E10176 1A) 40 0.28 dbj|D48409|RICS14588A Rice cDNA, partial sequence (S14588 1A). 40 0.28 dbj|C26556|C26556 Rice cDNA, partial sequence (C12586 1A) 40 0.28 dbi|D47831|RICS13548A Rice cDNA, partial sequence (S13548\_1A). 40 0.28 dbi|C72152|C72152 Rice cDNA, partial sequence (E1094 3A) 40 0.28 dbi|D46553|RICS11305A Rice cDNA, partial sequence (S11305 2A). 40 0.28 gb|AI028926|AI0289 (and many others of similar score)

# **SEQ ID NO:565**

emb|X68308|OOLPLIP O.ovis mRNA for lipoprotein lipase gb|AE000660|HUAE000660 Homo sapiens T-cell receptor alpha delta... 40 1.2 emb|AL022333|HS474I12 Human DNA sequence \*\*\* SEQUENCING IN PROG... 38 4.6 emb|Z12618|CFTRG C.fasciculata gene encoding trypanothione redu... 38 4.6 gb|M81651|HUMSEMIIB Human semenogelin II (SEMGII) gene, complet... gb|M96980|HUMMYT1A Homo sapiens myelin transcription factor 1 (... 38 4.6 gb|U89688|ACU89688 Acanthamoeba castellanii myosin-I binding pr... 38 4.6 gb|AC002497|AC002497 Human Cosmid g1940a142 from 7q31.3, comple... 38 4.6 gb|M81652|HUMSMNGLN Homo sapiens semenogelin II mRNA, complete ... gb|M25665|HUMNCF1A Human neutrophil cytosol factor 1 (NCF-47k) ... 38 4.6 gb|M73325|TRFTRPREDC Crithidia fasciculata trypanothione reduct... 38 4.6 gb|M73324|TRFTRPREDB Crithidia fasciculata trypanothione reduct... 38 4.6 emb|X92589|MMSEMIIGN M.mulatta semenogelin II gene 38 4.6 emb|Z47556|HSSG1SG2 H.sapiens genes for semenogelin I and semen... 38 4.6 gb|AC004753|AC004753 Homo sapiens chromosome 16, cosmid clone R... 38 4.6 gb|M55067|HUMNADPHO Human 47-kD autosomal chronic granulomatous... 38 4.6

gb|M73323|TRFTRPREDA Crithidia fasciculata trypanothione reduct... 38 4.6

# **HUMAN ESTs**

gb R11942 R11942 yf54c05.r1 Homo sapiens cDNA clone 25950 5'. 656 0.0
gb AA366384 AA366384 EST77326 Pancreas tumor III Homo sapiens c 470 e-130
gb T12566 T12566 CHR90086 Homo sapiens genomic clone P94_24 5' 133 5e-29
gb R37032 R37032 yf54c05.s1 Homo sapiens cDNA clone 25950 3'. 44 0.036
gb AA661650 AA661650 nv02h12.s1 NCI_CGAP_Pr22 Homo sapiens cDNA 38 2.2
gb AA261982 AA261982 zs20d03.rl NCI_CGAP_GCB1 Homo sapiens cDNA 38 2.2
gb AA588219 AA588219 no24c11.s1 NCI_CGAP_Pr22 Homo sapiens cDNA 38 2.2
gb AA250891 AA250891 zs06c06.r1 NCI_CGAP_GCB1 Homo sapiens cDNA 38 2.2
gb AA244177 AA244177 nc05a02.rl NCI_CGAP_Prl Homo sapiens cDNA 38 2.2
gb AA715147 AA715147 nv10d05.s1 NCI_CGAP_Pr22 Homo sapiens cDNA 38 2.2
gb AA659887 AA659887 nv03a10.s1 NCI_CGAP_Pr22 Homo sapiens cDNA 38 2.2
gb AA627890 AA627890 nq70a08.s1 NCI_CGAP_Pr22 Homo sapiens cDNA 38 2.2
gb AA603596 AA603596 np27b11.s1 NCI_CGAP_Pr22 Homo sapiens cDNA 38 2.2
gb AA613738 AA613738 np25h09.s1 NCI_CGAP_Pr22 Homo sapiens cDNA 38 2.2
gb AA715248 AA715248 nv10h06.s1 NCI_CGAP_Pr22 Homo sapiens cDNA 38 2.2
gb AI038487 AI038487 ow25d12.x1 Soares_parathyroid_tumor_NbHPA 38 2.2
gb AA252786 AA252786 zs26f10.rl NCI_CGAP_GCB1 Homo sapiens cDNA 38 2.2
gb AA287819 AA287819 zs50h04.rl NCI_CGAP_GCB1 Homo sapiens cDNA 38 2.2
gb AA564176 AA564176 nj04c08.s1 NCI_CGAP_Pr21 Homo sapiens cDNA 38 2.2
gb AA643870 AA643870 np26h07.s1 NCI_CGAP_Pr22 Homo sapiens cDNA 38 2.2
gb AA280371 AA280371 zt05f07.r1 NCI_CGAP_GCB1 Homo sapiens cDNA 38 2.2
gb R00687 R00687 ye78h08.r1 Homo sapiens cDNA clone 123903 5' s 38 2.2
gb AA587820 AA587820 nj06h05.s1 NCI_CGAP_Pr21 Homo sapiens cDNA 38 2.2
gb AA588443 AA588443 no22c11.s1 NCI_CGAP_Pr22 Homo sapiens cDNA 38 2.2
gb AA568385 AA568385 nl88f06.sl NCI_CGAP_Co10 Homo sapiens cDNA 38 2.2
gb AA281831 AA281831 zt06c08.rl NCI_CGAP_GCB1 Homo sapiens cDNA 38 2.2
gb AA700438 AA700438 zj74b08.s1 Soares fetal liver spleen 1NFLS 38 2.2
gb AA689530 AA689530 ns66e07.r1 NCI_CGAP_Pr22 Homo sapiens cDNA 38 2.2
gb AA688300 AA688300 nv14a09.s1 NCI_CGAP_Pr22 Homo sapiens cDNA 38 2.2
gb AA687962 AA687962 nv13h04.s1 NCI_CGAP_Pr22 Homo sapiens cDNA 38 2.2
gb AA526586 AA526586 ni96f11.s1 NCI_CGAP_Pr21 Homo sapiens cDNA 38 2.2
gb AA642589 AA642589 nq73f04.s1 NCI_CGAP_Pr22 Homo sapiens cDNA 38 2.2
gb AA541594 AA541594 ni89g07.s1 NCI_CGAP_Pr21 Homo sapiens cDNA 38 2.2
gb AA278713 AA278713 zs76h02.rl NCI_CGAP_GCB1 Homo sapiens cDNA 38 2.2
gb T58661 T58661 ya94a07.r1 Homo sapiens cDNA clone 69300 5' si 38 2.2
gb AA689473 AA689473 ns66e07.s1 NCI_CGAP_Pr22 Homo sapiens cDNA 38 2.2
gb AA459023 AA459023 aa26a09.r1 NCI_CGAP_GCB1 Homo sapiens cDNA 38 2.2

dbj|C76752|C76752 Mus musculus 3.5-dpc blastocyst cDNA 3'-end s... 60 2e-07 gb|AA123048|AA123048 mn32g01.rl Beddington mouse embryonic regi... 36 3.2 gb|AA616529|AA616529 vo10e01.rl Barstead mouse myotubes MPLRB5 ... 36 3.2 gb|AA254370|AA254370 va13h09.rl Soares mouse lymph node NbMLN M... 36 3.2 gb|AA537288|AA537288 vk46c04.rl Soares mouse mammary gland NbMM... 36 3.2 gb|AA462365|AA462365 vg74c05.rl Soares mouse NbMH Mus musculus ... 36 3.2 gb|AA589462|AA589462 vl47g07.sl Stratagene mouse skin (#937313)... 36 3.2 gb|AA968017|AA968017 uh06h10.rl Soares mouse hypothalamus NMHy ... 36 3.2

dbi|C93868|C93868 Dictyostelium discoideum slug cDNA, clone SSL809 36 2.8 gb|AA531984|AA531984 TgESTzz46b06.r1 TgME49 invivo Bradyzoite c... 36 2.8 gb|N60418|N60418 TgESTzy07a10.rl TgRH Tachyzoite cDNA Toxoplasm... 36 2.8 gb|H32045|H32045 EST106774 Rat PC-12 cells, untreated Rattus sp... 36 2.8 gb|AA956789|AA956789 UI-R-E1-fr-h-01-0-UI.s1 UI-R-E1 Rattus nor... 36 2.8 gb|H33275|H33275 EST109117 Rat PC-12 cells, NGF-treated (9 days... 36 2.8 gb|AA531938|AA531938 TgESTzz45b08.r1 TgME49 invivo Bradyzoite c... 36 2.8 dbi|D41507|RICS4044A Rice cDNA, partial sequence (S4044\_1A). gb|AA799411|AA799411 EST188908 Normalized rat heart, Bento Soar... 36 2.8 gb|AA519671|AA519671 TgESTzz27c10.r1 TgME49 invivo Bradyzoite c... 36 2.8 dbj|D40678|RICS2786A Rice cDNA, partial sequence (S2786 1A). 36 2.8 gb|AA012430|AA012430 TgESTzz22b12.r1 TgME49cDNA Toxoplasma gond... 36 2.8 dbi|D40551|RICS2612A Rice cDNA, partial sequence (S2612 1A). 36 2.8 gb|AI008452|AI008452 EST202903 Normalized rat embryo, Bento Soa... 36 2.8 dbj|D41253|RICS3620A Rice cDNA, partial sequence (\$3620 1A). gb|AA923843|AA923843 UI-R-A1-dr-f-04-0-UI.s1 UI-R-A1 Rattus nor... 36 2.8 gb|AA799410|AA799410 EST188907 Normalized rat heart, Bento Soar... 36 2.8

We claim:

1. A method of diagnosing a disorder characterized by expression of a human cancer associated antigen precursor coded for by a nucleic acid molecule, comprising:

contacting a biological sample isolated from a subject with an agent that specifically binds to the nucleic acid molecule, an expression product thereof, or a fragment of an expression product thereof complexed with an HLA molecule, wherein the nucleic acid molecule is a NA Group 1 nucleic acid molecule, and

determining the interaction between the agent and the nucleic acid molecule or the expression product as a determination of the disorder.

- The method of claim 1, wherein the agent is selected from the group consisting of
- (a)
  a nucleotide acid molecule comprising NA group 1 nucleic acid molecules
  or a fragment thereof,
  - (b)
    a nucleic acid molecule comprising NA group 3 nucleic acid molecules or a fragment thereof,
  - (c)
    a nucleic acid molecule comprising NA group 17 nucleic acid molecules
    or a fragment thereof,
- 25 (d)
  an antibody that binds to an expression product of NA group 1 nucleic acids,
- (e)
  an antibody that binds to an expression product of NA group 3 nucleic acids,

(f)

an antibody that binds to an expression product of NA group 17 nucleic

acids,

5

(g)

and agent that binds to a complex of an HLA molecule and a fragment of an expression product of a NA group 1 nucleic acid,

10 (h)

an agent that binds to a complex of an HLA molecule and a fragment of an expression product of a NA group 3 nucleic acid, and

(I)

an agent that binds to a complex of an HLA molecule and a fragment of an expression product of a NA group 17 nucleic acid.

- 3. The method of claim 1, wherein the disorder is characterized by expression of a plurality of human cancer associated antigen precursors and wherein the agent is a plurality of agents, each of which is specific for a different human cancer associated antigen precursor, and wherein said plurality of agents is at least 2, at least 3, at least 4, at least 6, at least 7, or at least 8, at least 9 or at least 10 such agents.
- 4. The method of claims 1-3, wherein the agent is specific for a human cancer associated antigen precursor that is a breast, a gastric, a lung, a prostate, a renal or a colon cancer associated antigen precursor.
- 5. A method for determining regression, progression or onset of a condition characterized by expression of abnormal levels of a protein encoded by a nucleic acid molecule that is a NA Group 1 molecule, comprising

monitoring a sample, from a patient who has or is suspected of having the condition, for a parameter selected from the group consisting of

**(I)** 5 the protein, (ii) a peptide derived from the protein, 10 (iii) an antibody which selectively binds the protein or peptide, and (iv) cytolytic T cells specific for a complex of the peptide derived from the 15 protein and an MHC molecule, as a determination of regression, progression or onset of said condition. The method of claim 5, wherein the sample is a body fluid, a body 6. effusion or a tissue. 20 7. The method of claim 5, wherein the step of monitoring comprises contacting the sample with a detectable agent selected from the group consisting of (a) an antibody which selectively binds the protein of (I), or the peptide of (ii), 25 (b) a protein or peptide which binds the antibody of (iii), and 30 (c)

		a cell which presents the complex of the peptide and MHC molecule of
	(iv).	
5		
	8.	The method of claim 7, wherein the antibody, the protein, the peptide or
	the cell is labeled wit	th a radioactive label or an enzyme.
	9.	The method of claim 5, comprising assaying the sample for the peptide.
10	10	
	10.	The method of claim 5, wherein the nucleic acid molecule is a NA Group
	3 molecule.	
	11.	The method of claims & mhanning the model, and the last of the las
15	11. 11 molecule.	The method of claim 5, wherein the nucleic acid molecule is a NA Group
13	11 molecule.	
	12.	The method of claim 5, wherein the nucleic acid molecule is a NA Group
	12 molecule.	The method of claim 3, wherein the nucleic acid molecule is a NA Group
20	13.	The method of claim 5, wherein the nucleic acid molecule is a NA Group
	13 molecule.	· · · · · · · · · · · · · · · · · · ·
	14.	The method of claim 5, wherein the nucleic acid molecule is a NA Group
	14 molecule.	-
25		
	15.	The method of claim 5, wherein the nucleic acid molecule is a NA Group
	15 molecule.	
	16.	The method of claim 5, wherein the nucleic acid molecule is a NA Group
30	16 molecule.	

- 17. The method of claim 5, wherein the protein is a plurality of proteins, the parameter is a plurality of parameters, each of the plurality of parameters being specific for a different of the plurality of proteins.
- A pharmaceutical preparation for a human subject comprising
  an agent which when administered to the subject enriches selectively the
  presence of complexes of an HLA molecule and a human cancer associated antigen, and
  a pharmaceutically acceptable carrier, wherein the human cancer
  associated antigen is a fragment of a human cancer associated antigen precursor encoded by a
  nucleic acid molecule comprises a NA Group 1 molecule.
  - 19. The pharmaceutical preparation of claim 18, wherein the agent comprises a plurality of agents, each of which enriches selectively in the subject complexes of an HLA molecule and a different human cancer associated antigen.
  - 20. The pharmaceutical preparation of claim 19, wherein the plurality is at least two, at least three, at least four or at least 5 different such agents.

- The pharmaceutical preparation of claim 18, wherein the nucleic acid molecule is a NA Group 3 nucleic acid molecule.
  - 22. The pharmaceutical preparation of claim 18, wherein the agent is selected from the group consisting of
- (1) an isolated polypeptide comprising the human cancer associated antigen, or a functional variant thereof,
  - (2) an isolated nucleic acid operably linked to a promoter for expressing the isolated polypeptide, or functional variant thereof,
  - (3) a host cell expressing the isolated polypeptide, or functional variant thereof, and

- (4) isolated complexes of the polypeptide, or functional variant thereof, and an HLA molecule.
- The pharmaceutical preparation of claims 18-22, further comprising an adjuvant.
  - 24. The pharmaceutical preparation of claim 18, wherein the agent is a cell expressing an isolated polypeptide comprising the human cancer associated antigen or a functional variant thereof, and wherein the cell is nonproliferative.

25. The pharmaceutical preparation of claim 18, wherein the agent is a cell expressing an isolated polypeptide comprising the human cancer associated antigen or a functional variant thereof, and wherein the cell expresses an HLA molecule that binds the polypeptide.

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- 26. The pharmaceutical preparation of claim 18, wherein the agent is at least two, at least three, at least four or at least five different polypeptides, each coding for a different human cancer associated antigen or functional variant thereof.
- 20 27. The pharmaceutical preparation of claim 18, wherein the agent is a PP Group 2 polypeptide.
  - 28. The pharmaceutical preparation of claim 18, wherein the agent is a PP Group 3 polypeptide or a PP Group 4 polypeptide.

25

- 29. The pharmaceutical preparation of claim 25, wherein the cell expresses one or both of the polypeptide and HLA molecule recombinantly.
- The pharmaceutical preparation of claim 25, wherein the cell is nonproliferative.

30

A composition comprising
an isolated agent that binds selectively a PP Group 1 polypeptide.

- 32. The composition of matter of claim 31, wherein the agent binds selectively a PP Group 3 polypeptide.
  - 33. The composition of matter of claim 31, wherein the agent binds selectively a PP Group 11 polypeptide.
- 10 34. The composition of matter of claim 31, wherein the agent binds selectively a PP Group 12 polypeptide.
  - 35. The composition of matter of claim 31, wherein the agent binds selectively a PP Group 13 polypeptide.
  - 36. The composition of matter of claim 31, wherein the agent binds selectively a PP Group 14 polypeptide.
- The composition of matter of claim 31, wherein the agent binds selectively a PP Group 15 polypeptide.
  - 38. The composition of matter of claim 31, wherein the agent binds selectively a PP Group 16 polypeptide.
- 25 39. The composition of claims 31-38, wherein the agent is a plurality of different agents that bind selectively at least two, at least three, at least four, or at least five different such polypeptides.
  - 40. The composition of claims 31-38, wherein the agent is an antibody.

The composition of claim 39, wherein the agent is an antibody. 41. A composition of matter comprising 42. a conjugate of the agent of claims 31-41 and a therapeutic or diagnostic agent. The composition of matter of claim 42, wherein the conjugate is of the 43. agent and a therapeutic or diagnostic that is a toxin. A pharmaceutical composition comprising an isolated nucleic acid 10 44. molecule selected from the group consisting of: (1)NA Group 1 molecules, and (2) 15 NA Group 2 molecules, and a pharmaceutically acceptable carrier. 45. The pharmaceutical composition of claim 44, wherein the isolated nucleic acid molecule comprises a NA Group 3 or NA Group 4 molecule. 20 46. The pharmaceutical composition of claim 44, wherein the isolated nucleic acid molecule comprises at least two isolated nucleic acid molecules coding for two different polypeptides, each polypeptide comprising a different human cancer associated antigen. The pharmaceutical composition of claims 44-46 further comprising an 25 47. expression vector with a promoter operably linked to the isolated nucleic acid molecule. The pharmaceutical composition of claims 44-46 further comprising a host 48. cell recombinantly expressing the isolated nucleic acid molecule.

30

49.	A pharmaceutical composition comprising
	an isolated polypeptide comprising a PP Group 1 or a PP Group 2
polypeptide, and	
	a pharmaceutically acceptable carrier.

- 50. The pharmaceutical composition of claim 49, wherein the isolated polypeptide comprises a PP Group 3 or a PP Group 4 polypeptide.
- 10 51. The pharmaceutical composition of claim 49, wherein the isolated polypeptide comprises at least two different polypeptides, each comprising a different human cancer associated antigen.
  - 52. The pharmaceutical composition of claim 49, wherein the isolated polypeptides are PP Group 11 polypeptides or HLA binding fragments thereof.
    - 53. The pharmaceutical composition of claim 49, wherein the isolated polypeptides are PP
      Group 12 polypeptides or HLA binding fragments thereof.

20

- 54. The pharmaceutical composition of claim 49, wherein the isolated polypeptides are PP Group 13 polypeptides or HLA binding fragments thereof.
- 55. The pharmaceutical composition of claim 49, wherein the isolated polypeptides are PP Group 14 polypeptides or HLA binding fragments thereof.
  - 56. The pharmaceutical composition of claim 49, wherein the isolated polypeptides are PP Group 15 polypeptides or HLA binding fragments thereof.

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67.

is a Group 16 molecule or a fragment thereof.

57.	The pharmaceutical composition of claim 49, wherein the isolated			
polypeptides are PP Group 16 polypeptides or HLA binding fragments thereof.				
58.	The pharmaceutical composition of claims 49-57, further comprising an			
adjuvant.				
59.	An isolated nucleic acid molecule comprising a NA Group 3 molecule.			
60.	An isolated nucleic acid molecule comprising a NA Group 4 molecule.			
61.	The isolated nucleic acid molecule of claims 59-60, wherein the molecule			
is a Group 11 molecule or a fragment thereof.				
62.	The isolated nucleic acid molecule of claims 59-60, wherein the molecule			
is a Group 12 molecule or a fragment thereof.				
63.	The isolated nucleic acid molecule of claims 59-60, wherein the molecule			
is a Group 13 molecule or a fragment thereof.				
64.	The isolated nucleic acid molecule of claims 59-60, wherein the molecule			
is a Group 14 molecule or a fragment thereof.				
65.	The ignited pyologo acid molecule of claims 50 00 mb milest			
65. The isolated nucleic acid molecule of claims 59-60, wherein the molecule is a Group 15 molecule or a fragment thereof.				
66.	The isolated nucleic acid molecule of claims 59-60, wherein the molecule			

An isolated nucleic acid molecule selected from the group consisting of

(a)

a fragment of a nucleic acid selected from the group of nucleic acid consisting of SEQ ID NOs presenting nucleic acid sequences among SEQ ID NOs. 1-816, of sufficient length to represent a sequence unique within the human genome, and identifying a nucleic acid encoding a human cancer associated antigen precursor,

(b)

complements of (a),

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provided that the fragment includes a sequence of contiguous nucleotides which is not identical to any sequence selected from the sequence group consisting of

(1) sequences having the GenBank accession numbers of Table 1 (correct?),

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- (2) complements of (1), and
- (3) fragments of (1) and (2).

68. The isolated nucleic acid molecule of claim 67, wherein the sequence of contiguous nucleotides is selected from the group consisting of:

20

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(1)

at least two contiguous nucleotides nonidentical to the sequence group,

(2)

at least three contiguous nucleotides nonidentical to the sequence group,

(3)

at least four contiguous nucleotides nonidentical to the sequence group,

(4)

at least five contiguous nucleotides nonidentical to the sequence group,

(5)

30

at least six contiguous nucleotides nonidentical to the sequence group,

(6)

at least seven contiguous nucleotides nonidentical to the sequence group.

69. The isolated nucleic acid molecule of claim 67, wherein the fragment has a size selected from the group consisting of at least: 8 nucleotides, 10 nucleotides, 12 nucleotides, 14 nucleotides, 16 nucleotides, 18 nucleotides, 20, nucleotides, 22 nucleotides, 24 nucleotides, 26 nucleotides, 28 nucleotides, 30 nucleotides, 50 nucleotides, 75 nucleotides, 100 nucleotides, and 200 nucleotides.

329

- 10 70. The isolated nucleic acid molecule of claim 67, wherein the molecule encodes a polypeptide which, or a fragment of which, binds a human HLA receptor or a human antibody.
- 71. An expression vector comprising an isolated nucleic acid molecule of claims 59, 60, 61, 62, 63, 64, 65, 66, 67, 68, 69 or 70 operably linked to a promoter.
  - 72. An expression vector comprising a nucleic acid operably linked to a promoter, wherein the nucleic acid is a NA Group 2 molecule.
- 20 73. An expression vector comprising a NA Group 1 or Group 2 molecule and a nucleic acid encoding an HLA molecule.
  - 74. A host cell transformed or transfected with an expression vector of claims 71, 72, or 73.

75. A host cell transformed or transfected with an expression vector of claim 71 or claim 72 and further comprising a nucleic acid encoding HLA.

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76. An isolated polypeptide encoded by the isolated nucleic acid molecule of claims 59, 60, 61, 62, 63, 64, 65, or 66.

- 77. A fragment of the polypeptide of claim 76 which is immunogenic.
- 78. The fragment of claim 77, wherein the fragment, or a portion of the fragment, binds HLA or a human antibody.

- 79. An isolated fragment of a human cancer associated antigen precursor which, or portion of which, binds HLA or a human antibody, wherein the precursor is encoded by a nucleic acid molecule that is a NA Group 1 molecule.
- 10 80. The fragment of claim 79, wherein the fragment is part of a complex with HLA.
  - 81. The fragment of claim 79, wherein the fragment is between 8 and 12 amino acids in length.

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- 82. An isolated polypeptide comprising a fragment of the polypeptide of claim 76 of sufficient length to represent a sequence unique within the human genome and identifying a polypeptide that is a human cancer associated antigen precursor.
- 20 83. A kit for detecting the presence of the expression of a human cancer associated antigen precursor comprising
  - a pair of isolated nucleic acid molecules each of which consists essentially of a molecule selected from the group consisting of
- 25 (a) a 12-32 nucleotide contiguous segment of the nucleotide sequence of any of the NA Group 1 molecules and
  - (b) complements of ("a"), wherein the contiguous segments are nonoverlapping.

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- 84. The kit of claim 83, wherein the pair of isolated nucleic acid molecules is constructed and arranged to selectively amplify an isolated nucleic acid molecule that is a NA Group 3 molecule.
- 5 85. A method for treating a subject with a disorder characterized by expression of a human cancer associated antigen precursor, comprising

administering to the subject an amount of an agent, which enriches selectively in the subject the presence of complexes of an HLA molecule and a human cancer associated antigen, effective to ameliorate the disorder, wherein the human cancer associated antigen is a fragment of a human cancer associated antigen precursor encoded by a nucleic acid molecule selected from the group consisting of

- (a) a nucleic acid molecule comprising NA group 1 nucleic acid molecules,
- (b) a nucleic acid molecule comprising NA group 3 nucleic acid molecules,
- (c)
  a nucleic acid molecule comprising NA group 17 nucleic acid molecules.
- 86. The method of claim 85, wherein the disorder is characterized by expression of a plurality of human cancer associated antigen precursors and wherein the agent is a plurality of agents, each of which enriches selectively in the subject the presence of complexes of an HLA molecule and a different human cancer associated antigen.
- 87. The method of claim 86, wherein the plurality is at least 2, at least 3, at least 4, or at least 5 such agents.

- 88. The method of claims 85-87, wherein the agent is an isolated polypeptide selected from the group consisting of PP Group 1, PP Group 2, PP Group 3, PP Group 4, PP Group 5, PP Group 6, PP Group 7, PP Group 8, PP Group 9, PP Group 10, PP Group 11, PP Group 12, PP Group 13, PP Group 14, PP Group 15, PP Group 16 and PP Group 17 polypeptides.
- 89. The method of claims 85-88, wherein the disorder is cancer.
- 90. A method for treating a subject having a condition characterized by
  expression of a human cancer associated antigen precursor in cells of the subject, comprising:
  - (I) removing an immunoreactive cell containing sample from the subject,
- contacting the immunoreactive cell containing sample to the host cell under conditions favoring production of cytolytic T cells against a human cancer associated antigen which is a fragment of the precursor,

introducing the cytolytic T cells to the subject in an amount effective to lyse cells which express the human cancer associated antigen, wherein the host cell is transformed or transfected with an expression vector comprising an isolated nucleic acid molecule operably linked to a promoter, the isolated nucleic acid molecule being selected from

the group of nucleic acid molecules consisting of NA Group 1, NA Group 2, NA Group 3, NA Group 4, NA Group 5, NA Group 6, NA Group 7, NA Group 8, NA Group 9, NA Group 10, NA Group 11, NA Group 12, NA Group 13, NA Group 14, NA Group 15, NA Group 16, and NA Group 17.

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	91.	The method of claim 90, wherein the host cell recombinantly expresses an
	HLA molecule which	binds the human cancer associated antigen.
	92.	The method of claim 90, wherein the host cell endogenously expresses an
5	HLA molecule which	binds the human cancer associated antigen.
	93.	A method for treating a subject having a condition characterized by
	expression of a huma	n cancer associated antigen precursor in cells of the subject, comprising:
10		(I)
10		
	• • • • • •	identifying a nucleic acid molecule expressed by the cells associated with
	said condition, where	in said nucleic acid molecule is a NA Group 1 molecule
		(ii)
15		transfecting a host cell with a nucleic acid selected from the group
	consisting of	<b>5</b>
•		
		(a) the nucleic acid molecule identified,
20		
		(b)
		a fragment of the nucleic acid identified which includes a segment coding
	for a human cancer as	ssociated antigen,
25		
		(c)
		deletions, substitutions or additions to (a) or (b), and
		actions, substitutions of auditions to (a) of (b), and

(d) degenerates of (a), (b), or (c);

(iii)

culturing said transfected host cells to express the transfected nucleic acid molecule, and;

(iv)

introducing an amount of said host cells or an extract thereof to the subject
effective to increase an immune response against the cells of the subject associated with the
condition.

94. The method of claim 93, further comprising:

15

(a)

identifying an MHC molecule which presents a portion of an expression product of the nucleic acid molecule,

- wherein the host cell expresses the same MHC molecule as identified in

  (a) and wherein the host cell presents an MHC binding portion of the expression product of the nucleic acid molecule.
- 95. The method of claim 93, wherein the immune response comprises a B-cell response or a T cell response.
  - 96. The method of claim 95, wherein the response is a T-cell response which comprises generation of cytolytic T-cells specific for the host cells presenting the portion of the expression product of the nucleic acid molecule or cells of the subject expressing the human cancer associated antigen.

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- 97. The method of claim 93, wherein the nucleic acid molecule is a NA Group 3 molecule.
- 98. The method of claims 93 or 94, further comprising treating the host cells to render them non-proliferative.
  - 99. A method for treating or diagnosing or monitoring a subject having a condition characterized by expression of an abnormal amount of a protein encoded by a nucleic acid molecule that is a NA Group 1 molecule, comprising
- administering to the subject an antibody which specifically binds to the protein or a peptide derived therefrom, the antibody being coupled to a therapeutically useful agent, in an amount effective to treat the condition.
- The method of claim 99, wherein the antibody is a monoclonal antibody.
  - 101. The method of claim 100, wherein the monoclonal antibody is a chimeric antibody or a humanized antibody.
- 102. A method for treating a condition characterized by expression in a subject
  20 of abnormal amounts of a protein encoded by a nucleic acid molecule that is a NA Group 1
  nucleic acid molecule, comprising

administering to a subject a pharmaceutical composition of any one of claims 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, 30, 44, 45, 46, 47, 48, 49, 50, 51, 52, 53, 54, 55, 56, 47, and 58 in an amount effective to prevent, delay the onset of, or inhibit the condition in the subject.

- 103. The method of claim 102, wherein the condition is cancer.
- The method of claims 102-103, further comprising first identifying that the subject expresses in a tissue abnormal amounts of the protein.

- 105. A method for treating a subject having a condition characterized by expression of abnormal amounts of a protein encoded by a nucleic acid molecule that is a NA Group 1 nucleic acid molecule, comprising
- (I) identifying cells from the subject which express abnormal amounts of the protein;
  - (ii) isolating a sample of the cells;
  - (iii) cultivating the cells, and
  - (iv) introducing the cells to the subject in an amount effective to provoke an immune response against the cells.

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106. The method of claim 105, wherein the cells express a protein selected from the group consisting of a PP Group 11 protein, a PP Group 12 protein, a PP Group 13 protein, PP Group 14 protein, a PP Group 15 protein and a PP Group 16 protein.

15

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- 107. The method of claim 105, further comprising rendering the cells non-proliferative, prior to introducing them to the subject.
- 108. A method for treating a pathological cell condition characterized by aberrant expression of a protein encoded by a nucleic acid molecule that is a NA Group 1 nucleic acid molecule, comprising

administering to a subject in need thereof an effective amount of an agent which inhibits the expression or activity of the protein.

- 25 109. The method of claim 108, wherein the agent is an inhibiting antibody which selectively binds to the protein and wherein the antibody is a monoclonal antibody, a chimeric antibody or a humanized antibody.
- The method of claim 108, wherein the agent is an antisense nucleic acid molecule which selectively binds to the nucleic acid molecule which encodes the protein.

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	111.	The method of claim 108, wherein the nucleic acid molecule is a NA
	Group 3 nucleic ac	cid molecule.
	112.	A composition of matter useful in stimulating an immune response to a
5	plurality of a prote	ein encoded by nucleic acid molecules that are NA Group 1 molecules,
	comprising	
		a plurality of peptides derived from the amino acid sequences of the
	proteins, wherein	the peptides bind to one or more MHC molecules presented on the surface of
	the cells which ex	press an abnormal amount of the protein.
10		
	113.	The composition of matter of claim 112, wherein at least a portion of the
	plurality of peptid	es bind to MHC molecules and elicit a cytolytic response thereto.
	114.	The composition of matter of claim 113, further comprising an adjuvant.
15	115.	The composition of matter of claim 114, wherein said adjuvant is a
	saponin, GM-CSF	F, or an interleukin.
	116.	An isolated antibody which selectively binds to a complex of:
20		(i)
		a peptide derived from a protein encoded by a nucleic acid molecule that is
	a NA Group 1 mc	elecule and
25		(ii)
		and an MHC molecule to which binds the peptide to form the complex,
	wherein the isolat	ed antibody does not bind to (I) or (ii) alone.
	117.	The antibody of claim 116, wherein the antibody is a monoclonal
30	antibody, a chime	eric antibody or a humanized antibody.

TINIQQI.SOLPKQIILETIIRKTKQSEGELAYLERINERE.GKFKGRGNDRREKLQSFDSPERKRIKYSRETDS..DRKLVDKEDID 1050 VINIQQLSDLIIKQMIDI YRRSHLSEQFLEALELRERE, MKYRDRAAERREKYGI PEPPEPKRKKQFDAGTV... NYEQPTKDGID 742 THIQQLSCLINCOLLATIERALLSHIFTEN LEKNIME CAKYRORABERREKYGIPEPPEPKRKYGGISTASVDFEQPTRIGLC 316 DEPARATION OF THE PROTECT OF THE PRO KENSPPPPVVVPDLICLICEYGGOSDYEEEEEEGYPPPQPPVTAQPQKREEGTKKENBEDKLTDWNKLACLLCRRQFPNKEVL 970 PELVINUDEEHPLKRGLVAAYSGDSDNEB..........ELVENLESEEEKLADHKKMACLLCRRQFPNKDAL 662 815 389 T SEGUCIVI GAT GARK GTGLGY JIIPSLASSEE A GGAARGPS V GAS GATSKROSNETYRDAVARAWEARYKELD HENIGNKMLQAMGWREGSGLGKKCOCTTAPTEAQVRLKGAGLGAKGSAYGLSGADSYKDAVRKAMPARFIEME simigsrafioamgakegsglgrkkogtvypteaotrvrbsglgargssygvtstesyketlhktavtrfhed() 11. -171 - 71 DXS8237E HER CHEZO 13. LIU 1. PASSES VE HY 1.0-12 LUCALS LUČATS LUCALS

Ergune

1 400

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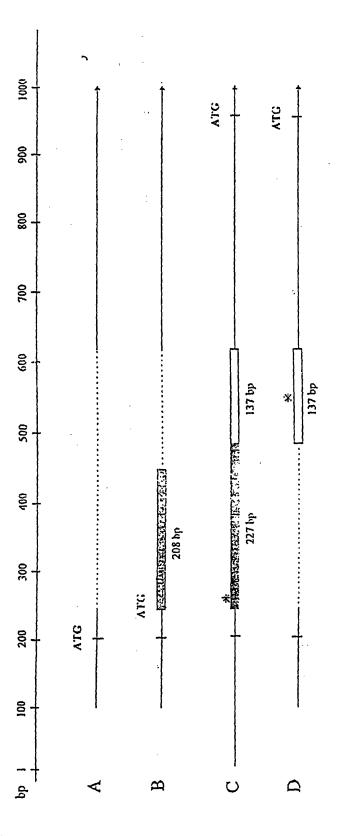
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ANGATANGTCRCAGGTTTGTGGAGGAGAAGTTGAGATGGTKKTTGTGTTTAARGAAGAAGAKKKKTGTKKAGTTTGTTKKGGGKTAAGACAKKKGA Q d r s q l s g b r q s s u a g l, f k b 'l g g l l g i e q d t u TTACAGAAGCATGAAGTGATGTGGATGATAGGTKKCAKAAAGUNAATGYTTGGCTATGKCAAGTGYTTTKKAGAKGGGAAAACTGCC Y R S M E Y R D V D H R L P G S Q H F G Y G Q S K S F F E G K T A R S S D F G S R D S S O L D L R G L D I H S G D F R D R R G P P R SATTIPAGGGCAMAGNATGGGATCTIGTANGANTTANGANGANGANGANGANGANTATTAGATTACATTANGANGCTCHA ACANGATAGAGAACATTGTGGTATGTGAACAKKAGACAKKACACACACACACATAGGATAGAAAGKGCTTT IVGCATTGAAGKGAGAA O D R B K S G H N V N R R E B S T H II II T R R R F G I Q R G B EXCEPTABLISACION TO CHARACION CONTROCATOR CONTROCATION TO THE TOTAL TO THE CONTROL OF THE CONTRO GAPOTYSGGGGATTYT CGACCTYCT AACHGAACTYCALLYCALLYCATYCGARGAAGAAAGGAAGGATTGCTCCLYCGGTTCGAACAAGATTATTCCTCCTT × \_; < ~ ţ, = ĸ × 25 = ĸ c/; :: ے ~ ບ -Œ ÷ 2 = Ο. **:** D Y R G R R GTACKICA. 1.14 167 30 334 \$C\$ 234 267 301 201 367 101 7 67

figure 2

467	A T K E E I L R A F R T P D G K P V K $R_{\rm eff}$ D L K E Y N T G Y D Y G Y	
<u> </u>		<u> </u>
534	CTATCAAGCCTGGATTTTTGGTACTGGAAAACATGAAACATTAGTGGGACTATCTTCCTTC	1890
567	NYGCANGGANGANTINATANGCITACCITCAGCCTCAGANANCATCCATACCAGACAGAGANANGAGCCCANGCAGCCCTANGACCAGGTCATAA E A K Q E L I T Y P Q P Q R T S L F A P 5 E K Q P R Q P L R P A P K	1400
169	ESTANCETORACCEAGGAGGAGGAGGAGGAGGAGGAGGAGGAGGAGGAGGAGG	2000
6 55	PYDACTITCCHANGACHANGAGHAGHCHATCHTATCHTCHACACGCCACCATCGATAGAAAACTATCATCTAAGGTATCTATC	2100
1.93	CACCACCERACTEMPORTHERANGTER TRACTER CONTRACTOR TO THE TOTAL TO THE TOTAL	22.00
733	CIATGGCTTTNITGACTCTGTAGGGCTCTTUTGGTGTGTGTGAAGATCTTAGAAACCTIGATCCACCATTYAGGATTGGGAAGATAAAAA '' G F I D L D S H V E A L R V V K I L Q H L D P P F S I D G K H V	2.300
734	CONTRADACTORECACTURANDACANAGANATONTONO STATEMENTO CANTACATACATACATACARANAAANAAANAAAAAAAAAA	3400
191	GAGATGGGARANATTCAGACTGGATACAAAATCGACAAGACAAGACAAGA	2500
833	TORECETIBELACIANTATION PROCEDUATACOUR CONTRACTORION TO THE BUTTORION TRACTORION TRACTORION TO THE	3000
834	WAGCCHCUNGTGAGGANGTCANGTARCAACAARGAANGTCAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAA	2 100
867	CONCEGNACIOCAMENTACIONE PROPERTATION CONTRACTORISMA AND A RESERVED FOR THE PROPERTY OF THE PRO	2800
931	PUTGNTCGGCTCTTGGGTGAATALGGAGAGAGAGAGAGAAGAAGAAGAAGAAGAAGAAGAGCTCGCCCACAGCCCCCCCC	2900
931	CARANGCGAGAGGAGCAAACCAAGAAGGAGAAAAAAAAAA	3000



Transcript Variant B

AAGSAGGAGGGGGGGGGGGTTGGCCCCTAGGTACTGCTATAACCAGAATTTGCTTATAAAAGGATTTAGTTGTGGGCCCTCTTGATAAAAAGAGATGTGGGGGGATTCTCGAC 1200 CTACTANCACNACTORACCTITICANGCCTITICACONTOTICACIONICICICALICACIONATORACCOCACANCECOCCANAGICATAGARATICATA (1145) ATTTAGIGGENGU 360 (152) CANGRAGATTGTTGTCCCGGGTGG..

Fig. 30

## Figure 35.

227bp excn:
GACTGGGTGAAAGCTTTTCTGCAGCAGTGATGTTAAAAACCTTGTGTTGACTTTCCTCG
TGTTCTGAAACTAAC
AGAACTGGACCTTTTCGGACTGGGTGAAAGCTTTTCTGCAGCAGTCATGTTGAAAACC
TTGTGTTGAAATGGGAGCATAAAAGTTTACTCCGCCACTTCGTCTTAAAATAGCAAAAC
TTTGCTGTTTTCTGCAG

## 137bc exon:

ATCTAGGACCTTGTTACAGAACTCTGCCAAAAAAAAATGTTTACAGAAGAATGTGCTGT GATTAGAGAAGAATA

TGCTGGTGTGTAGATTTCAAACTCTCTGGACAATATGAATAACACTGTCTTTGTTTCTAC

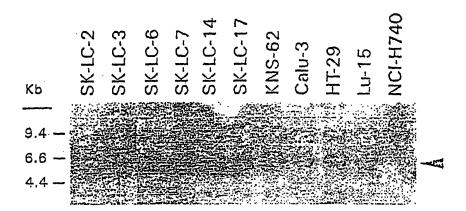


Figure 4

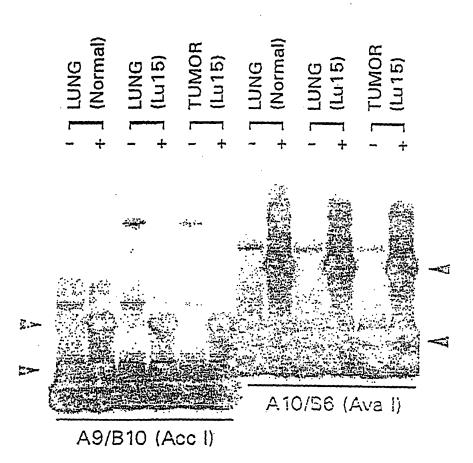


Figure 5

## SEQUENCE LISTING

<110> Ludwig Institute for Cancer Research
Old, Lloyd J.
Scanlan, Matthew J.
Stockert, Elisabeth
Gure, Ali
Chen, Yao-Tseng
Gout, Ivan
O'Hare, Michael
Obata, Yuichi
Pfreundschuh, Michael
Tureci, Ozlem
Sahin, Ugur

## <120> CANCER-ASSOCIATED NUCLEIC ACIDS AND POLYPEPTIDES

- <130> L0461/7039/JRV/ERG
- <140> Unknown
- <141> 1998-07-15
- <150> U.S. 08/896,164
- <151> 1997-07-17
- <150> U.S. 60/061,599
- <151> 1997-10-10
- <150> U.S. 60/061,765
- <151> 1997-10-10
- <150> U.S. 08/948,705
- <151> 1997-10-10
- <150> U.S. SNU (LUD5506.1)
- <151> 1998-06-22
- <150> U.K. 9721697.2
- <151> 1997-10-11
- <160> 816
- <170> FastSEQ for Windows Version 3.0
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- <400> 1

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540

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240

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2040

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                                                                     3720
aanttetggt tgcaateeet eecegteeea cantgeeece catttgagta cacegeacaa
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gtcaaacgnt aggnagtttg nataaaacca atttttctaa nttgttgntc atttgttgta
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aaaacctaag tetgtggttg cacegecagg tgctcctaag aaagagcatg taaatgtagt
                                                                      180
attcattggg cacgtanatg ctggcaagtc aaccattgga ggacaaataa tgtatttgac
                                                                      240
tggaatggtt gacaaaagga cgcttgaaaa gtatgaaaga gaagctaaag agaaaaacag
                                                                      300
agaaacttgg tacttgtctt gggccttaga cacaaatcag gaagaacgag acaagggtaa
                                                                      360
aacagtagaa gtgggtcgtg cctattttga aaccgaaaag aacatttcac aattctagat
                                                                      420
atgaateeca gaacaetgag etcaaaaeee aaageecaga atttgaaget caaagtteen
                                                                      480
aattccanga aggtgcggag atgcttctga accccgagga aaagatcctt tgaatatctc
                                                                      540
cgtaggagtt cacccctgg actccttcac tcaggggttt ggggagcacc cacaggggac
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<212> DNA

<213> Homo Sapiens

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                                                                       120
accttectga agacetgete geacactgea tecettgeag teagtteeag etegtgeega
                                                                       180
atteggeacg agetegtgee gaatteggea egagggaage actaeteeca gegetgggee
                                                                       240
caggaggacc tgctggagga gcagaaggat ggggcccggg cagcggctgt ggctgacaag
                                                                       300
aagaaaggcc tcatggggcc actgaccgaa ctggacacta aagatgtgga tgccctgctg
                                                                       360
aagaagtetg aggeecagea tgaacageeg gaagatggat geecetttgg tgeectgaeg
                                                                       420
cagcgcctcc tgcaggccct ggtggaggaa aatattattt tttccc
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      <212> DNA
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gccacagete ecageettee tgcageagat gcagaateca gacacaetat cagecatgte
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aaacccaaga gcaatgcagg ctttaatgca gatccagcag gggctacaga cattagccac
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cattcaattg aaatgcagga tggtgcactg ccattccaag ttccatcttc ctggcagatc
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agcacagggt tccccagaag ttcatatcct ggattacagg tgtatgaaac catggtacca
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tacagaaagt ttgatgaatg tgtagcagga gactcctttg tattttccca ggttttagcc
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actgctccca aatgataagg agggtgagga gtcacatatg gaacttccat catgtcgtct
                                                                       360
tettgeteaa aatateeetg gteatetttg agtttagtae agteteeaaa atetatatga
                                                                       420
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                                                                       180
aggacettgt aacatgeeca aaceaggtgt atttgacttg atcaacaagg ccaaatggga
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cgcatggaat gcccttggca gcctgcccaa ggaagctgcc aggcagaact atgtggattt
                                                                       300
ggtgtccagt ttgagtcctt cattggaatc ctctagtcag gtggagcctg gaacagacag
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gaaatcaact gggtttgaaa ctctggtggt gacctccgaa gatggcatca caaagatcat
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gttcaaccgg cccaaaaaga aaaatgccat aaacactgag atgtatcatg aaattatgcg
                                                                       480
tgcacttaaa gctgccagca aggatgactc aatcatcact gttttaacag gaaatggtga
                                                                       540
ctattacagt agtgggaatg atctgactaa cttcactgat attccccctg gtggagtana
                                                                       600
ggagaaagct aaaaataatg ccgttttact gaagggaatt tgtgggctgt tttatagaat
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ttcctaagcc tctgattgc
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attgatettt ccagagtgee gggaateagt aaagaettaa gagaagtggt eetatetget
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qaaaatqatg aattctatgc taataatatg tacctgaact ttgctgagat tggtagcaat
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ataaagaatc tcatggaaga ttttcagaag aagaaaccaa aagaacagca aaaactagaa
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actqtttcaa aqcatqtqac aqtqqttqqa gaactqtctc gattqgtcaq tqaacqqaat
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ctgctggagg tttcagaggt tgagcaagaa ctggcctgtc aaaatgacca ttctaqtqct
                                                                       420
ctccagaata taaaaagget tetgcagaac eccaaagtga cagagtttga tgetgeeege
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ctggtgatgc tttatgcttt acattatgag cgacacagca gcaatagcct gccaggacta
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atgatggncc tcaggaataa aggtgtttct gagaagtatc gaaagctcgt gtctgcagtt
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gttgaatatg gtggtaaaac gagtcagagg aagtgacctc ctcagcccca aagatgctgt
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tggctatcac caaacaattc ctcaaaggg
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cccgcgaggc agagcttgca ataagccgag atcgtgccaa tgcactccag cctgggcaac
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agaaggagac actgtctcaa aaa
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caccagcacc accaagacct gattttgatg cttcaaggga aaaactacag aagcttqgtq
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cagcacatcc tattttgaga agagatttaa atttccatgt cttcttggaa tataatcaag
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gattgctttt ttgctacagt tttctgccaa atggcctagt tcctgagtac ctggaaacca
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gagagaaaga ggatccagga tgtacttgga tgaggaggcc tggcttatct aggaagtcgt
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tttgatagcc accaactgta cctgggtang caaagtcaga tttttgagaa nctttttcct
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gatttgaagt tttaattacc ttaatttcct tt
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ccaaceteca geccagagaa gecacaggaa etegttacag etgaggttge agetecatee
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acctcatett cagecaette etegeetgag ggteetteae etgeeegaee teeteggegt
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cgcaccagtg ctgatgtgga aattaggggt caagggactg gtcggccagg acaaccacca
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agnagecett cattgeneg
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            20
                                25
Pro Ser Val Arg Thr Gln Met Trp Leu Thr Glu Gln Leu Arg Thr Asn
                            40
Pro Leu Glu Gly Arg Asn Thr Glu Asp Ser Tyr Ser Leu Ala Pro Trp
                        55
Gln Gln Gln Gln Ile Glu Phe Arg Gln Gly Ser Glu Thr Pro Met Gln
                    70
                                        75
Val Leu Thr Gly Ser Ser Arg Gln Ser Tyr Ser Pro Gly Tyr Gln Asp
                85
                                    90
Phe Ser Lys Trp Glu Ser Met Leu Lys Lys Glu Gly Leu Leu Arg Gln
            100
                                105
Lys Glu Ile Val Asp Arg Gln Lys Gln Ile Thr His Leu Ile Arg Asp
                            120
Asn Glu Leu Pro Ala His Ala Met Leu Gly His Tyr Val Asn Cys Glu
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135

130

Asp Ser Tyr Val Ala Ser Leu His His 145

<210> 42

<211> 95

<212> PRT

<213> Homo Sapiens

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His Val Asn Asn His Ile Tyr Ile Lys Leu Tyr Asn Cys Thr Phe Leu 20 25 30

Thr Ala Leu Ser Gln Val Ala Leu Ser Phe Pro Ser Ile Asn Gly Leu 35 40 45

Ile Phe Val Ser Phe Ala Phe Phe Arg Val Val Asn Ser Tyr Cys Pro 50 55 60

Leu Gln Phe Val Gln Phe Leu Arg Cys Leu Leu Leu Leu Lys Arg Met 65 70 75 80

Leu Gly Glu Phe Ile Phe His Lys Glu Met Glu His Tyr Leu Lys 85 90 95

<210> 43

<211> 114

<212> PRT

<213> Homo Sapiens

<400> 43

Ser Lys Leu Leu Ser Gly Thr Ala Asp Gly Ala Asp Leu Arg Thr
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Val Asp Pro Glu Thr Gln Ala Arg Leu Glu Ala Leu Leu Glu Ala Ala 20 25 30

Gly Ile Gly Lys Leu Ser Thr Ala Asp Gly Lys Ala Phe Ala Asp Pro 35 40 45

Glu Val Leu Arg Arg Leu Thr Ser Ser Val Ser Cys Ala Leu Asp Glu 50 55 60

Ala Ala Ala Leu Thr Arg Met Arg Ala Glu Ser Thr Ala Asn Ala Gly 65 70 75 80

Gln Ser Asp Asn Arg Ser Leu Ala Glu Ala Cys Ser Gly Asp Val Ala 85 90 95

Val Arg Lys Leu Leu Ile Glu Gly Arg Ser Val Phe Glu Leu Pro Glu 100 105 110

Glu Gly

<210> 44

<211> 132

<212> PRT

<213> Homo Sapiens

<400> 44

Gly Glu Lys Glu Gln Asp Lys Pro Pro Asn Leu Val Leu Lys Asp Lys

1 5 10 15

Val Lys Pro Lys Gln Asp Thr Lys Tyr Asp Leu Ile Leu Asp Glu Gln

20 25 30

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Lys Thr His His Cys Ser Glu Glu Lys Glu Asp Glu Asp Tyr Met Pro
Ile Lys Asn Thr Asn Gln Asp Ile Tyr Arg Glu Met Gly Phe Gly His
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Tyr Glu Glu Glu Glu Ser Cys Trp Glu Lys Gln Lys Ser Glu Lys Arg
Asp Arg Thr Gln Asn Arg Ser Arg Ser Arg Ser Arg Glu Arg Asp Gly
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His Tyr Ser Asn Ser His Lys Ser Lys Tyr Gln Thr Asp Leu Tyr Glu
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                           120
Arg Glu Arg Ser
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      <211> 214
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Lys Ile Arg Lys Glu Met Arg Val Val Asp Arg Gln Ile Arg Asp Ile
           20
                               25
Gln Arg Glu Glu Lys Val Lys Arg Ser Val Lys Asp Ala Ala Lys
Lys Gly Gln Lys Asp Val Cys Ile Val Leu Ala Lys Glu Met Ile Arg
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Ser Arg Lys Ala Val Ser Lys Leu Ala Ser Lys Ala His Met Asn Ser
                   70
Val Leu Met Gly Met Lys Asn Gln Leu Ala Val Leu Arg Val Ala Gly
                                   90
Ser Leu Gln Lys Ser Thr Glu Val Met Lys Ala Met Gln Ser Leu Val
                               105
Lys Ile Pro Glu Ile Gln Ala Thr Met Arg Glu Leu Ser Lys Glu Met
                           120
Met Lys Ala Gly Ile Ile Glu Glu Met Leu Glu Asp Thr Phe Glu Ser
                       135
Met Asp Asp Gln Glu Glu Met Glu Glu Glu Ala Glu Met Glu Ile Asp
                   150
                                       155
Arg Ile Leu Phe Glu Ile Thr Ala Gly Ala Leu Gly Lys Ala Pro Ser
               165
                                   170
Lys Val Thr Asp Ala Leu Pro Glu Pro Glu Pro Pro Gly Ala Met Ala
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Ala Ser Glu Asp Glu Glu Glu Glu Glu Leu Glu Ala Met Gln Ser
                            200
Arg Leu Ala Thr Arg Ser
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     <211> 248
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<210> 47 <211> 177

<212> PRT

<213> Homo Sapiens

<400> 47

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 Cys
 His
 Tyr
 Cys
 Cys
 Lys
 Ser
 Cys
 Trp
 Asn
 Glu
 Tyr
 Leu

 1
 5
 5
 6
 10
 10
 7
 15
 15

 Thr
 Thr
 Arg
 Ile
 Glu
 Gln
 Asn
 Leu
 Val
 Leu
 Asn
 Cys
 Thr
 Cys
 Pro
 Ile
 Asn
 Leu
 Asn
 Pro
 Ile
 Asn
 Asn
 Ile
 Ile
 Asn<

115 Tyr Tyr Asp Gly Met Ser Val Glu Ala Lys His Leu Ala Lys Leu Ile 135 Ser Lys Arg Cys Pro Ser Cys Gln Ala Pro Ile Glu Asn Glu Gly Cys 150 155 Leu His Met Thr Cys Ala Lys Cys Asn His Gly Phe Cys Trp Arg Cys 17.0 Leu <210> 48 <211> 102 <212> PRT <213> Homo Sapiens <400> 48 Glu Lys Gly Leu His Ile Asp Gln Leu Val Cys Leu Val Leu Glu Ala Gln Lys Gly Pro Asn Pro Pro Gly Thr Leu Gly His Thr Val Ala Gly 25 Gly Val Ala Cys Thr Thr Thr Val Leu Ser Cys Leu His Leu Leu Ser 40 Gln Gly Tyr Lys Arg Asp Arg Pro Gln Ile Leu Met Tyr Ala Ala Pro 55 Pro Met Gly Pro Cys Arg Gly Ala His Phe Cys Gly Ser Ser Gln Thr 70 75 Ser Pro Pro Lys Pro Val Ala Thr Leu Ser Leu Leu Pro Cys Pro Leu 90 Pro Pro Leu Lys Asn Gly 100 <210> 49 <211> 179 <212> PRT <213> Homo Sapiens <400> 49 His Lys Pro Cys Asn Pro Arg Glu Lys Glu Arg Ile Gln Asn Ala Gly Gly Ser Val Met Ile Gln Arg Val Asn Gly Ser Leu Ala Val Ser Arg Ala Leu Gly Asp Tyr Asp Tyr Lys Cys Val Asp Gly Lys Gly Pro Thr 40 Glu Gln Leu Val Ser Pro Glu Pro Glu Val Tyr Glu Ile Leu Arg Ala Glu Glu Asp Glu Phe Ile Ile Leu Ala Cys Asp Gly Ile Trp Asp Val Met Ser Asn Glu Glu Leu Cys Glu Tyr Val Lys Ser Arg Leu Glu Val Ser Asp Asp Leu Glu Asn Val Cys Asn Trp Val Val Asp Thr Cys Leu 105 His Lys Gly Ser Arg Asp Asn Met Ser Ile Val Leu Val Cys Phe Ser 120 125 Asn Ala Pro Lys Val Ser Asp Glu Ala Val Lys Lys Asp Ser Glu Leu

130

<210> 50

<211> 163

<212> PRT

<213> Homo Sapiens

<400> 50

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<210> 51

Thr Leu Gln

<211> 164

<212> PRT

<213> Homo Sapiens

<400> 51

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 Ser Val
 Asp Cys
 Ser Asp Cys
 Trp Leu
 Pro Val
 Val
 Lys

 1
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 5
 10
 15
 15

 Phe Ile Glu Glu Gln Gln Fhe Glu Gln Tyr
 30
 30

100 105 Glu Asp Glu Asp Phe Lys Arg Gln Asp Ala Met Lys Glu Ser Ile Pro 120 Phe Ala Val Val Gly Ser Cys Gln Val Val Arg Asp Gly Gly Asn Arg 135 140 Pro Val Arg Gly Arg Arg Tyr Ser Trp Gly Asn Val Glu Val Asn His 150 155 Ile Ala Ile Ser

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305
                   310
                                      315
Pro Thr Ile Thr Val Leu Pro Ala Gln Leu Ala Pro Thr Lys Met Thr
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                        330
Gln Pro Ile Leu Gln Thr Ala Leu Pro Cys Gln Ile Leu Gly Gln Thr
                              345
Ser Leu Val Leu Thr Gln Val Thr Ser Gly Ser Thr Thr Val Ser Cys
                          360
Ser Pro Ile Thr Leu Ala Val Ala Gly Val Thr Asn His Gly Gln Lys
                     375
Arg Pro Leu Val Thr Pro Gln Ala Ala Pro Glu Pro Lys Arg Pro His
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                                      395
Ile Ala Gln Val Pro Glu Pro Pro Pro Lys Val Ala Asn Pro Pro Leu
               405
                                  410
Thr Pro Ala Ser Asp Arg Lys Lys Thr Lys Glu Gln Ile Ala His Leu
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Lys Ala Ser Phe Leu Gln Ser Gln Phe Pro Asp Asp Ala Glu Val Tyr
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Arg Leu Ile Glu Val Thr Gly Leu Ala Arg Ser Glu Ile Lys Lys Trp
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Phe Ser Asp His Arg Tyr Arg Cys Gln Arg Gly Ile Val His Ile Thr
                  470
                                      475
Ser Glu Ser Leu Ala Lys Asp Gln Leu Ala Ile Ala Ala Ser Arg His
                                  490
Gly Arg Thr Tyr His Ala Tyr Pro Asp Phe Ala Pro Gln Lys Phe Lys
                              505
Glu Lys Thr Gln Gly Gln Val Lys Ile Leu Glu Asp Ser Phe Leu Lys
                          520
Ser Ser Phe Pro Thr Gln Ala Glu Leu Asp Arg Leu Arg Val Glu Thr
   530 535
Lys Leu Ser Arg Arg Glu Ile Asp Ser Trp Phe Ser Glu Arg Arg Lys
                 550
                                     555
Leu Arg Asp Ser Met Glu Gln Ala Val Leu Asp Ser Met Gly Ser Gly
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              565
Gln Lys Arg Pro Arg Cys Gly Lys Pro Pro Met Val Leu Cys Leu Asp
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Ser Asn Ser Ser Pro Val Pro Ser
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Gly Gly Ser Leu Gly Asp Gly Arg Pro Pro Glu Glu Ser Ala His Glu
Met Met Glu Glu Glu Glu Ile Pro Lys Pro Lys Ser Val Val Ala
Pro Pro Gly Ala Pro Lys Lys Glu His Val Asn His Val Ala Gly Lys
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Ser Thr Ile Gly Gly Gln Ile Met Tyr Leu Thr Gly Met Val Asp Lys
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Arg Thr Leu Glu Lys Tyr Glu Arg Glu Ala Lys Glu Lys Asn Arg Glu
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| Secondary Seco

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<211> 155

<212> PRT

<213> Homo Sapiens

<400> 54

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Thr Lys Asp Val Asp Ala Leu Leu Lys Lys Ser Glu Ala Gln His Glu 115 120 125

Gln Pro Glu Asp Gly Cys Pro Phe Gly Ala Leu Thr Gln Arg Leu Leu 130 135 140

Gln Ala Leu Val Glu Glu Asn Ile Ile Phe Ser 145 150 155

<210> 55

<211> 112

<212> PRT

<213> Homo Sapiens

<400> 55

 Ser Glu Arg
 Ala Leu
 Ala Pro
 Arg
 Thr
 Tyr
 Arg
 Met
 Glu
 Thr
 Ala Arg
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Met Gln Ala Leu Met Gln Ile Gln Gln Gly Leu Gln Thr Leu Ala Thr 90 Glu Ala Pro Gly Leu Ile Pro Ser Phe Thr Pro Gly Val Gly 105 . 110 <210> 56 <211> 151 <212> PRT <213> Homo Sapiens <400> 56 Lys Phe Gly Met Pro Ile Asp Cys Gly Leu Pro Pro His Ile Asp Phe 5 10 Gly Asp Cys Thr Lys Leu Lys Asp Asp Gln Gly Tyr Phe Glu Gln Glu 25 Asp Asp Met Met Glu Val Pro Tyr Val Thr Pro His Pro Pro Tyr His 40 Leu Gly Ala Val Ala Lys Thr Trp Glu Asn Thr Lys Glu Ser Pro Ala Thr His Ser Ser Asn Phe Leu Tyr Gly Thr Met Val Ser Tyr Thr Cys Asn Pro Gly Tyr Glu Leu Leu Gly Asn Pro Val Leu Ile Cys Gln Glu 90 Asp Gly Thr Trp Asn Gly Ser Ala Pro Ser Cys Ile Ser Ile Glu Cys 100 105 Asp Leu Pro Thr Ala Pro Glu Asn Gly Phe Leu Arg Phe Thr Glu Thr 120 125 Ser Met Gly Ser Ala Val Gln Tyr Ser Cys Lys Pro Gly His Ile Leu 135 Ala Gly Ser Asp Leu Arg Leu <210> 57 <211> 220 <212> PRT <213> Homo Sapiens <400> 57 Ala Ala Phe Val Ser Glu Val Thr Ser Phe Pro Val Val Gln Leu His Met Asn Arg Thr Ala Met Arg Ala Ser Gln Lys Asp Phe Glu Asn Ser Ile Asn Gln Val Lys Leu Leu Lys Lys Asp Pro Gly Asn Glu Val Lys Leu Lys Leu Tyr Ala Leu Tyr Lys Gln Ala Thr Glu Gly Pro Cys Asn Met Pro Lys Pro Gly Val Phe Asp Leu Ile Asn Lys Ala Lys Trp Asp Ala Trp Asn Ala Leu Gly Ser Leu Pro Lys Glu Ala Ala Arg Gln Asn 90 Tyr Val Asp Leu Val Ser Ser Leu Ser Pro Ser Leu Glu Ser Ser Ser

Gln Val Glu Pro Gly Thr Asp Arg Lys Ser Thr Gly Phe Glu Thr Leu
115 120 125

Val Val Thr Ser Glu Asp Gly Ile Thr Lys Ile Met Phe Asn Arg Pro

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130
                        135
                                             140
Lys Lys Lys Asn Ala Ile Asn Thr Glu Met Tyr His Glu Ile Met Arg
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                                       155
Ala Leu Lys Ala Ala Ser Lys Asp Asp Ser Ile Ile Thr Val Leu Thr
                165
                                    170
Gly Asn Gly Asp Tyr Tyr Ser Ser Gly Asn Asp Leu Thr Asn Phe Thr
                                185
Asp Ile Pro Pro Gly Gly Val Glu Lys Ala Lys Asn Asn Ala Val Leu
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Leu Lys Gly Ile Cys Gly Leu Phe Tyr Arg Ile Ser
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Trp Pro Asp Leu Val His Thr Trp Ser Ser Glu Glu Ala Met Gly Ser
Cys Cys Ser Cys Pro Asp Lys Asp Thr Val Pro Asp Asn His Arg Asn
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Lys Phe Lys Val Ile Asn Val Asp Asp Gly Asn Glu Leu Gly Ser
Gly Ile Met Glu Leu Thr Asp Thr Glu Leu Ile Leu Tyr Thr Arg Lys
Arg Asp Ser Val Lys Trp His Tyr Leu Cys Leu Arg Arg Tyr Gly Tyr
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Asp Ser Asn Leu Phe Ser Phe Glu Ser Gly Pro Arg Cys Gln Thr Gly
Thr Arg Asn Leu Cys
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      <211> 43
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Ala His Gly Pro Gly Val Glu Pro Thr Ser Arg His Gln Lys Asn Asn
                                    10
Leu Ser Ser His Thr Val Arg Leu Glu Thr Arg Gly Gln Thr Glu
Asn Gln Glu Cys Leu Leu Cys Pro His Glu Glu
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      <213> Homo Sapiens
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Leu Asn Gln Trp Thr Tyr Gln Ala Met Val His Glu Leu Leu Gly Ile
Asn Asn Asn Arg Ile Asp Leu Ser Arg Val Pro Gly Ile Ser Lys Asp
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Leu Arg Glu Val Val Leu Ser Ala Glu Asn Asp Glu Phe Tyr Ala Asn
                           40
Asn Met Tyr Leu Asn Phe Ala Glu Ile Gly Ser Asn Ile Lys Asn Leu
                        55
Met Glu Asp Phe Gln Lys Lys Pro Lys Glu Gln Gln Lys Leu Glu
Ser Ile Ala Asp Met Lys Ala Phe Val Glu Asn Tyr Pro Gln Phe Lys
                                    90
Lys Met Ser Gly Thr Val Ser Lys His Val Thr Val Val Gly Glu Leu
                               105
Ser Arg Leu Val Ser Glu Arg Asn Leu Leu Glu Val Ser Glu Val Glu
                           120
Gln Glu Leu Ala Cys Gln Asn Asp His Ser Ser Ala Leu Gln Asn Ile
                       135
Lys Arg Leu Leu Gln Asn Pro Lys Val Thr Glu Phe Asp Ala Ala Arg
                                        155
Leu Val Met Leu Tyr Ala Leu His Tyr Glu Arg His Ser Ser Asn Ser
               165
                                   170
Leu Pro Gly Leu Met Met Leu Arg Asn Lys Gly Val Ser Glu Lys Tyr
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                                185
Arg Lys Leu Val Ser Ala Val Val Glu Tyr Gly Gly Lys Thr Ser Gln
                            200
Arg Lys
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Thr Pro Gly Pro Gly Ala Gly Phe Tyr Ala Cys Pro Ala Arg Pro Leu
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Val Ser Gly Ile Tyr Ser Phe Arg Trp Val Arg Gly Leu Ala Asp Gln
Glu Arg Asn Trp Gly Leu Ser Gln
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His Glu Ala Arg Leu Lys Arg Ala Ser Ala Pro Thr Phe Asp Asn Asp
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Tyr Ser Leu Ser Glu Leu Leu Ser Gln Leu Asp Ser Gly Val Ser Gln
                               25
Ala Val Glu Gly Pro Glu Glu Leu Ser Arg Ser Ser Ser Glu Ser Lys
                           40
Leu Pro Ser Ser Gly Ser Gly Lys Arg Leu Ser Gly Val Ser Ser Val
Asp Ser Ala Phe Ser Ser Arg Gly Ser Leu Ser Leu Ser Phe Glu Arg
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Glu Pro Ser Thr Ser Asp Leu Gly Thr Thr Asp Val Gln Lys Lys
                85
                                   90
Leu Val Asp Ala Ile Val Ser Gly Asp Thr Ser Lys Leu Met Lys Ile
Leu Gln Pro Gln Asp Val Asp Leu Ala Leu Asp Ser Gly Ala Ser Leu
                           120
Leu His Leu Ala Val Glu Ala Gly Gln Glu Glu Cys Ala Lys Trp Leu
                       135
Leu Leu Asn Asn Ala Asn Pro Asn Leu Ser Asn Arg Arg Gly Ser Thr
                   150
                            155
Pro Leu His Met Ala Val Glu Arg Arg Val Arg Gly Val Val Glu Leu
             165
                                   170
Leu Leu Ala Arg Ile Ser Val Asn Ala Lys Asp Glu Asp Gln Trp Thr
                               185
Ala Leu His Phe Ala Asn Gly Gly Val His Thr Ala Ala Val Gly Glu
                           200
Arg Leu Gly Gln Thr Lys Val Asp Phe Glu Gly Arg Thr Pro Met Gln
                       215
Val Gly Leu Pro Thr Thr Gly Lys Asn Ile Leu Arg Ile Leu
                230
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Arg Leu Gly Ala Ala Met Met Glu Gly Leu Asp Asp Gly Pro Asp Phe
                                   10
Leu Ser Glu Glu Asp Arg Gly Leu Lys Ala Ile Asn Val Asp Leu Gln
                               25
Ser Asp Ala Ala Leu Gln Val Asp Ile Ser Asp Ala Leu Ser Glu Arg
                           40
Asp Lys Val Lys Phe Thr Val His Thr Lys Ile Pro Pro Ala Pro Pro
                       55
Arg Pro Asp Phe Asp Ala Ser Arg Glu Lys Leu Gln Lys Leu Gly Glu
                   70
Gly Glu Gly Ser Met Thr Lys Glu Glu Phe Thr Lys Met Lys Gln Glu
Leu Glu Ala Glu Tyr Leu Ala Ile Phe Lys Lys Thr Val Ala Met His
                               105
Glu Val Phe Leu Cys Arg Val Ala Ala His Pro Ile Leu Arg Arg Asp
                          120
                                              125
Leu Asn Phe His Val Phe Leu Glu Tyr Asn Gln Asp Leu Ser Val Arg
                      135
Gly Lys
145
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Asn Glu Ser Ser Leu Glu Gln Val Tyr Thr Leu Lys Met Ser Phe Ile
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                          40
Ala Ser Asn Thr Tyr His Asn Gln Leu Tyr Lys Glu Gly Phe Leu
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                           40
Asp Arg Thr Ser Glu Glu Leu Thr Glu Ala Lys Thr Pro Thr Ser Ser
                       55
                                           60
Pro Glu Lys Pro Gln Glu Leu Val Thr Ala Glu Val Ala Ala Pro Ser
                   70
                                       75
Thr Ser Ser Ser Ala Thr Ser Ser Pro Glu Gly Pro Ser Pro Ala Arg
               85
                                   90
Pro Pro Arg Arg Thr Ser Ala Asp Val Glu Ile Arg Gly Gln Gly
           100
                               105
                                                   110
Thr Gly Arg Pro Gly Gln Pro Pro Gly Pro Lys Val Leu Arg Lys Leu
                           120
                                              125
Pro Gly Arg Leu Val Thr Val Val Glu Glu Lys Glu Leu Val Arg Arg
                    135
                                          140
Arg Arg Gln Gln Arg Gly Ala Ala Ser Thr Leu Val Pro Gly Val Ser
                                       155
Glu Thr Ser Ala Ser Pro Gly Ser Pro Ser Val Arg Ser Met Ser Gly
               165
                                  170
Pro Glu Ser Ser Pro Pro Ile Gly Gly Pro Cys Glu Ala Ala Pro Ser
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Ser Ser Leu Pro Thr Pro Pro
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                                                                     120
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                                                                     180
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                                                                     240
gttgtacaga agtcatatgg caatcaaaaa atttttttt gccctccccc ttgtgtatat
                                                                     300
cttatgggca gtggatggaa gaaaaaaaaa gaacaaatga aatgcgatgg ttgttctgaa
                                                                     360
cacagetete atecatgtge atttattggg ataggaaata gtgaccaaga aatgcagcag
                                                                      420
ctaaacttgg aaggaaagaa ctattgcaca gccaaaacat tgtacatatc tgattcagac
                                                                      480
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aaqcaaaaqc acttcatttt ttctgtaaag gtgttctatg gcaacqgtqa tgacattggt
                                                                      540
gtgttcctca gcaagtagat aaaagtcatc tccaaacctt ccaaaaagaa gcagtcattg
                                                                      600
aaaaatqctg acttatgcat tgtctcagga acaaaggtgg ctctgtttaa tcgactacga
                                                                      660
tcccagacag ttagtaccag atacttgcat gtagaaggag gtaattttca tgccagttca
                                                                      720
cagcagtggg gagcatttta cattcaattc ttggatgatg atggatcaga aggagaagaa
                                                                      780
ttcacaqtct gagatgccta cattcattat ggacaaacat gcaaacttgt gtgctcagtt
                                                                      840
actggcatgg cactcccaag attgataatt atgaaagttg ataagcatac cgcattattg
                                                                      900
gatgcagatg atcctgtgtc acaactccat aaatgtgcat tttaccttaa ggatacagaa
                                                                      960
agaatgtatt tgtgcctttc tcaagaaaga ataattcaat ttcaggccac tccatgtcca
                                                                     1020
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ggacagaatt tcactccaaa tttacgagtg tggtttgggg gggtagaagc tgaaactatg
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<211> 729

<212> PRT

<213> Homo Sapiens

<400> 67

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225					230										
		Luc	: 17al	Levi				· T		235		_,	_		240
	, vu	. برت	, val	245	Hom	. 1111	ser	Leu			ггуз	Phe	e Ası		Lys
T.VS	: Tle	Tle	ם דו			λαν	There	· T 011	250					255	Glu
			260		. Der	Asp	TYL			ııyı	ASP	Ser			Glu
Val	Δen	Gla			Thr	17-1	60.	265				_	270		
Vul	. AGII	275		Ser	1111	vai			ATA	GIA	Pro			Thr	Phe
G1 <sub>1</sub>	1727			T 110	T1.	T1.	280			_		285	-		
GIC	290	PLC	ASII	nys.	TTE			Arg	Ala	гга			Leu	Lys	Ile
Δer			ui.c	Tira	~1 <sub>~</sub>	295					300				
305	, 116	neu	nis	пуя			Ser	GLY	Asn			Туг	Gly	' Val	Phe
		Tri o	Tara	T	310			<b>~</b> 3 ·	_	315					320
Met	. Leu	nis	гуу	ъуs 325	THE	val	Asn	GIN			Thr	Ile	Tyr		Ile
G) n	Aen	λαη	7~~			Mob	*	**- 1	330		_,			335	
GIII	Asp	мар	340		ьуѕ	Met	Asp			GLY	Thr	Gly			His
λαη	Tla	Dro			<b>01</b>	<b>a</b> 1	<b>3</b>	345			_		350		
ASII	Ile	355	cys	GIU	GIU	GIY			ьeи	Gin	Leu			Phe	Arg
Lan	7~~			7	<b>~1</b> -	M-4-	360		_		_	365			
шеи	Arg 370	ьуѕ	пλя	ASII	GIII			гÀг	Leu	Ile			Met	His	Ser
Dha			T10	T	T	375		• -	_	_	380				
385	Ile	GIII	116	ьys	ъуs	ьys	Thr	Asn	Pro			Asn	Asp	Pro	Lys
		Larg	Lon	Dro	390	<i>α</i> 1	<b>~1</b>	3	~1	395		_			400
JCI	Met	шуз	Leu	405	GIII	GIU	GIN	Arg			Pro	Tyr	Pro		Glu
Δla	Ser	Thr	Thr		Dro	C3	Com	TT	410			_		415	
	Ser	1111	420	FIIE	PIO	GIU	ser		ьeu	Arg	Thr	Pro		Met	Pro
Pro	Thr	Thr		Car	Car	cor	Dho	425	m\	<b>T</b>		_	430		_
		435	110	Der	Ser	261	440	Pile	Thr	гÀг	ьуs		GLu	Asp	Thr
Tle	Ser		Met	λen	Nen	Dha		71	Mak	a1	<b>-1</b>	445	_		_
	450	275	1100	ASII	АЗР	455	MEC	Arg	Met	GIN		Leu	ьys	Glu	Gly
Ser	His	Phe	Pro	Glv	Dro		Mot	The	C 0 ×	T1 ~	460	<b>D</b>			_
465				<b>U</b> -1	470	riic	Mec	1111	ser	475		PLO	Ala	GIU	
	Pro	His	Thr	Pro		Met	Pro	Dro	Sar			C	0		480
				485	0111	1.00	110	FIU	490	TILL	PLO	ser	ser		Phe
Leu	Thr	Thr	Leu		Pro	Δτα	I.e.11	Lare		Cl.,	Dwo	<b>G1</b>	<b>~</b> 1	495	_
			500	-75		9	u	505	1111	Giu	PIO	GIU		vai	ser
Ile	Glu	Asp		Ala	Gln	Ser	Δsn		Tare	Glu	17-1	Mob	510	<b>.</b>	-
		515					520	ДСЦ	шуз	GIU	vai	525	val	ьeu	Asn
Ala	Thr	Glu	Ser	Phe	Val	Tvr		Pro	Laze	Glin	Gl n	723	T	W	D1
	530					535		-10	Ly 5	GIU	540	пås	гуя	Mec	Pne
His	Ala	Thr	Val	Ala	Thr		Asn	Glu	Val	Dho	240	3757	T	1707	Dh.
545					550					555		Val	гуѕ	vaı	
Asn	Ile	Asp	Leu				Phe	Thr				Tlo	Tla	71-	560
		-		565		-4			570	<b></b> ,5	Lys	116	116		тте
Ala	Asn	Tyr	Val	Cvs	Arg	Asn	Glv	Phe		Glu	Val	Тъгъ	Dro	575 Dha	mb
		•	580	- 2			1	585		<b></b>	val	Tyr	590	Pile	THE
Leu	Val	Ala	Asp	Val	Asn	Ala	αzA		Asn	Met	Glu	Tla	Dro	Tura	<b>~</b> 1
		595	-				600					605	110	Буз	GIY
Leu	Ile	Arq	Ser	Ala	Ser	Val		Pro	Lvs	Tle	Δen	Gln	Lou	Crea	Com
	610	-			-	615			_, •		620		<b></b> =u	СуБ	SET
Gln	Thr	Lys	Gly	Ser	Phe		Asn	Glv	٧a٦	Phe	Glu	Va 1	Hie	Laza	Tue
625		-	-	-	630			1		635	JIU	va <sub>1</sub>	****	пÃр	_
Asn	Val	Arq	Gly	Glu		Thr	Tvr	Tvr	Glu		Gln	Δan	Δen	ጥኩ~	640
		-	4	645			- 2 -	- , ~	650			vah	นอน		GTÀ
Lys	Met	Glu	Val		Val	His	Glv	Ara		Agn	Thr	Tla	λοη	655 Cva	C1
-			660	_			1	665			- ***	-TC	670	cys	GIU
													3,0		

Glu Gly Asp Lys Leu Lys Leu Thr Ser Phe Glu Leu Ala Pro Lys Ser 680 Gly Asn Thr Gly Glu Leu Arg Ser Val Ile His Ser His Ile Lys Val 695 Ile Lys Thr Lys Lys Asn Lys Lys Asp Ile Leu Asn Pro Asp Ser Ser 710 Met Glu Thr Ser Pro Asp Phe Phe 725 <210> 68 <211> 754 <212> PRT <213> Homo Sapiens <400> 68 Met Ala Ser Val Pro Ala Leu Gln Leu Thr Pro Ala Asn Pro Pro Pro 10 Pro Glu Val Ser Asn Pro Lys Lys Pro Gly Arg Val Thr Asn Gln Leu Gln Tyr Leu His Lys Val Val Met Lys Ala Leu Trp Lys His Gln Phe 40 Ala Trp Pro Phe Arg Gln Pro Val Asp Ala Val Lys Leu Gly Leu Pro 55 Asp Tyr His Lys Ile Ile Lys Gln Pro Met Asp Met Gly Thr Ile Lys 70 Arg Arg Leu Glu Asn Asn Tyr Tyr Trp Ala Ala Ser Glu Cys Met Gln 90 Asp Phe Asn Thr Met Phe Thr Asn Cys Tyr Ile Tyr Asn Lys Pro Thr 105 Asp Asp Ile Val Leu Met Ala Gln Thr Leu Glu Lys Ile Phe Leu Gln 120 Lys Val Ala Ser Met Pro Gln Glu Glu Gln Glu Leu Val Val Thr Ile 135 140 Pro Lys Asn Ser His Lys Lys Gly Ala Lys Leu Ala Ala Leu Gln Gly 150 155 Ser Val Thr Ser Ala His Gln Val Pro Ala Val Ser Ser Val Ser His 165 170 Thr Ala Leu Tyr Thr Pro Pro Pro Glu Ile Pro Thr Thr Val Leu Asn 180 185 Ile Pro His Pro Ser Val Ile Ser Ser Pro Leu Leu Lys Ser Leu His 200 Ser Ala Gly Pro Pro Leu Leu Ala Val Thr Ala Ala Pro Pro Ala Gln 215 Pro Leu Ala Lys Lys Lys Gly Val Lys Arg Lys Ala Asp Thr Thr Thr 230 235 Pro Thr Pro Thr Ala Ile Leu Ala Pro Gly Ser Pro Ala Ser Pro Pro 250 Gly Ser Leu Glu Pro Lys Ala Ala Arg Leu Pro Pro Met Arg Arg Glu 265 Ser Gly Arg Pro Ile Lys Pro Pro Arg Lys Asp Leu Pro Asp Ser Gln 280 Gln Gln His Gln Ser Ser Lys Lys Gly Lys Leu Ser Glu Gln Leu Lys 295 300 His Cys Asn Gly Ile Leu Lys Glu Leu Leu Ser Lys Lys His Ala Ala 310 315

Tyr	Ala	Trp	Pro	Phe 325	Tyr	Lys	Pro	Val	Asp 330	Ala	Ser	Ala	Leu	Gly 335	Leu
His	Asp	Tyr	His 340	Asp	Ile	Ile	Lys	His 345	Pro	Met	Asp	Leu	Ser 350	Thr	Val
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	_	-		Lys 405			_		410				-	415	
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	450			Glu		455					460				_
465				Arg	470		_			475					480
				Glu 485 Lys					490			_		495	
			500	Arg				505					510	_	_
		515		Arg	_	_	520	_		_		525	-	-	-
	530			Gly		535			-	-	540	-	-		
545				Gly	550					555					560
				565 Pro					570				_	575	
	PLO				~		-1-							w	
Ara			580		Asp	Glu	Lvs	585 Ara	G1n	Leu	Ser	Leu	590 Asp	Tle	Asn
	Pro	Met 595	580 Ser	Tyr			600	Arg				605	Asp		
Lys	Pro Leu 610	Met 595 Pro	580 Ser Gly		Lys	Leu 615	600 Gly	Arg Arg	Val	Val	His 620	605 Ile	Asp Ile	Gln	Ala
Lys Arg 625	Pro Leu 610 Glu	Met 595 Pro Pro	580 Ser Gly Ser	Tyr Glu Leu	Lys Arg 630	Leu 615 Asp	600 Gly Ser	Arg Arg Asn	Val Pro	Val Glu 635	His 620 Glu	605 Ile Ile	Asp Ile Glu	Gln Ile	Ala Asp 640
Lys Arg 625 Phe	Pro Leu 610 Glu Glu	Met 595 Pro Pro	580 Ser Gly Ser Leu	Tyr Glu	Lys Arg 630 Pro	Leu 615 Asp Ser	600 Gly Ser Thr	Arg Arg Asn Leu	Val Pro Arg 650	Val Glu 635 Glu	His 620 Glu Leu	605 Ile Ile Glu	Asp Ile Glu Arg	Gln Ile Tyr 655	Ala Asp 640 Val
Lys Arg 625 Phe Leu	Pro Leu 610 Glu Glu Ser	Met 595 Pro Pro Thr	580 ser Gly ser Leu Leu 660	Tyr Glu Leu Lys 645	Lys Arg 630 Pro Lys	Leu 615 Asp Ser Lys	600 Gly Ser Thr	Arg Asn Leu Arg 665	Val Pro Arg 650 Lys	Val Glu 635 Glu Pro	His 620 Glu Leu Tyr	605 Ile Ile Glu Thr	Asp Ile Glu Arg Ile 670	Gln Ile Tyr 655 Lys	Ala Asp 640 Val Lys
Lys Arg 625 Phe Leu Pro	Pro Leu 610 Glu Glu Ser Val	Met 595 Pro Pro Thr Cys Gly 675	580 Ser Gly Ser Leu Leu 660 Lys	Tyr Glu Leu Lys 645 Arg	Lys Arg 630 Pro Lys Lys	Leu 615 Asp Ser Lys Glu	600 Gly Ser Thr Pro Glu 680	Arg Asn Leu Arg 665 Leu	Val Pro Arg 650 Lys Ala	Val Glu 635 Glu Pro Leu	His 620 Glu Leu Tyr	605 Ile Ile Glu Thr Lys 685	Asp Ile Glu Arg Ile 670 Lys	Gln Ile Tyr 655 Lys Arg	Ala Asp 640 Val Lys Glu
Lys Arg 625 Phe Leu Pro	Pro Leu 610 Glu Glu Ser Val Glu 690	Met 595 Pro Pro Thr Cys Gly 675 Lys	580 Ser Gly Ser Leu Leu 660 Lys	Tyr Glu Leu Lys 645 Arg	Lys Arg 630 Pro Lys Lys Gln	Leu 615 Asp Ser Lys Glu Asp 695	600 Gly Ser Thr Pro Glu 680 Val	Arg Asn Leu Arg 665 Leu Ser	Val Pro Arg 650 Lys Ala Gly	Val Glu 635 Glu Pro Leu Gln	His 620 Glu Leu Tyr Glu Leu 700	605 Ile Ile Glu Thr Lys 685 Asn	Asp Ile Glu Arg Ile 670 Lys Ser	Gln Ile Tyr 655 Lys Arg	Ala Asp 640 Val Lys Glu Lys
Lys Arg 625 Phe Leu Pro Leu Lys 705	Pro Leu 610 Glu Glu Ser Val Glu 690 Pro	Met 595 Pro Pro Thr Cys Gly 675 Lys	Ser Gly Ser Leu 660 Lys Arg	Tyr Glu Leu Lys 645 Arg Thr Leu Lys Ser	Lys Arg 630 Pro Lys Lys Gln Ala 710	Leu 615 Asp Ser Lys Glu Asp 695 Asn	600 Gly Ser Thr Pro Glu 680 Val	Arg Asn Leu Arg 665 Leu Ser Lys	Val Pro Arg 650 Lys Ala Gly	Val Glu 635 Glu Pro Leu Gln Glu 715	His 620 Glu Leu Tyr Glu Leu 700 Ser	605 Ile Ile Glu Thr Lys 685 Asn	Asp Ile Glu Arg Ile 670 Lys Ser Ser	Gln Ile Tyr 655 Lys Arg Thr	Ala Asp 640 Val Lys Glu Lys Gln 720
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                            40
Ser Glu Gly Arg Pro Arg Arg Thr Asp Leu Thr Val Leu Val Ala His
                        55
Asn Asp Asp Pro Thr Asp Gln Met Phe Val Phe Phe Pro Glu Glu Pro
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                                        75
Lys Val Gly Ile Lys Thr Ile Lys Val Tyr Cys Gln Arg Met Gln Glu
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Glu Asn Ile Thr Arg Ala Leu Ile Val Val Gln Gln Gly Met Thr Pro
                                105
Ser Ala Lys Gln Ser Leu Val Asp Met Ala Pro Lys Tyr Ile Leu Glu
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                                                125
Gln Phe Leu Gln Gln Glu Leu Leu Ile Asn Ile Thr Glu His Glu Leu
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                                            140
Val Pro Glu His Val Val Met Thr Lys Glu Glu Val Thr Glu Leu Leu
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Ala Arg Tyr Lys Leu Arg Glu Asn Gln Leu Pro Arg Ile Gln Ala Gly
                                   170
Asp Pro Val Ala Arg Tyr Phe Gly Ile Lys Arg Gly Gln Val Val Lys
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Ile Ile Arg Pro Ser Glu Thr Ala Gly Arg Tyr Ile Thr Tyr Arg Leu
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Val Gln
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Ser Phe Gln Glu Leu Glu Asp Lys Lys Glu Leu Ser Glu Glu Ser Glu
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Asp Glu Glu Leu Gln Leu Glu Glu Phe Pro Met Leu Lys Thr Leu Asp
Pro Lys Asp Trp Lys Asn Gln Asp His Tyr Ala Val Leu Gly Leu Gly
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His Val Arg Tyr Thr Ala Thr Gln Arg Gln Ile Lys Ala Ala His Lys 100 105 Ala Met Val Leu Lys His His Pro Asp Lys Arg Lys Ala Ala Gly Glu 120 Pro Ile Lys Glu Gly Asp Asn Asp Tyr Phe Thr Cys Ile Thr Lys Ala 135 140 Tyr Glu Met Leu Ser Asp Pro Val Lys Arg Arg Ala Phe Asn Ser Val 150 155 Asp Pro Thr Phe Asp Asn Ser Val Pro Ser Lys Ser Glu Ala Lys Asp 165 170 Asn Phe Phe Gln Val Phe Ser Pro Val Phe Glu Arg Asn Ser Arg Trp 180 185 Ser Asn Lys Lys Asn Val Pro Lys Leu Gly Asp Met Asn Ser Ser Phe 200 Glu Asp Val Asp Ala Phe Tyr Ser Phe Trp Tyr Asn Phe Asp Ser Trp 215 Arg Glu Phe Ser Tyr Leu Asp Glu Glu Glu Lys Glu Lys Ala Glu Cys 230 235 Arg Asp Glu Arg Lys Trp Ile Glu Lys Gln Asn Arg Ala Thr Arg Ala 245 250 Gln Arg Lys Lys Glu Glu Met Asn Arg Ile Arg Thr Leu Val Asp Asn 265 Ala Tyr Ser Cys Asp Pro Arg Ile Lys Lys Phe Lys Glu Glu Lys 280 Ala Lys Lys Glu Ala Glu Lys Lys Ala Lys Ala Glu Ala Arg Arg Lys 295 300 Glu Gln Glu Ala Lys Glu Lys Gln Arg Gln Ala Glu Leu Glu Ala Val 310 315 Arg Leu Ala Lys Glu Lys Glu Glu Glu Glu Val Arg Gln Gln Ala Leu 325 330 Leu Ala Lys Lys Glu Lys Asp Ile Gln Lys Lys Ala Ile Lys Lys Glu 345 Arg Gln Lys Leu Arg Asn Ser Cys Lys Ser Trp Asn His Phe Ser Asp 360 365 Asn Glu Ala Asp Arg Val Lys Met Met Glu Glu Val Glu Lys Leu Cys 375 Asp Arg Leu Glu Leu Ala Ser Leu Gln Gly Leu Asn Glu Ile Leu Ala 390 395 Ser Ser Thr Arg Glu Val Gly Lys Ala Ala Leu Glu Lys Gln Ile Glu 405 410 Glu Val Asn Glu Gln Met Arg Arg Glu Lys Glu Glu Ala Asp Ala Arg 420 425 Met Arg Gln Ala Ser Lys Asn Ala Glu Lys Ser Thr Gly Gly Ser Gly 440 445 Ser Gly Ser Lys Asn Trp Ser Glu Asp Asp Leu Gln Leu Leu Ile Lys 455 Ala Val Asn Leu Phe Pro Ala Gly Thr Asn Ser Arg Trp Glu Val Ile 470 475 Ala Asn Tyr Met Asn Ile His Ser Ser Ser Gly Val Lys Arg Thr Ala 490 Lys Asp Val Ile Ser Lys Ala Lys Ser Leu Gln Lys Leu Asp Pro His 505 Gln Lys Asp Asp Ile Asn Lys Lys Ala Phe Asp Lys Phe Lys Lys Glu 520 His Gly Val Ala Ser Gln Ala Asp Ser Ala Ala Pro Ser Glu Arg Phe

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		435					440					445			Gln
	450					455					460				Thr
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Gly	Met	Arg	Arg	Ser 485		Lys	Glu	Gln	Ala 490		Lys	Ile	Thr	Asn 495	Leu
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Phe	Asp 850	Gly	Leu	Arg	Lys	Lys 855		Thr	Ala	Met	Gln 860	Leu	Tyr	Glu	Суя
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Pro			Val	Ala	Leu			Gly	Leu	Ile	Asp	Ara	asp	Leu	Tvr
1025	5				1030	)				103	5				104
Arg	Ser	Leu	Asn	Asp 1045	Pro	Arg	Asp	Ser	Gln 1050		Asn	Phe	Val	Asp 1055	
Val	Thr	Lys	Lys 1060	Lys )	Val	Ser	Tyr	Val 106	Gln 5	Leu	Lys	Glu	Arg	Cys	Arg
Ile	Glu	Pro	His	Thr	Gly	Leu	Leu	Leu	Leu	Ser	Val	Gln	Lys	Ara	Ser
		1079	5				1080	)				1085	5		
Met	Ser 1090	1075 Phe )	Gln	Gly	Ile	Arg 1099	1080 Gln	) Pro	Val	Thr	Val	1085 Thr	5 Glu	Leu	Val
Met Asp	Ser 1090 Ser	1075 Phe )	Gln	Gly	Ile	Arg 1099	1080 Gln	) Pro	Val	Thr	Val	1085 Thr	5 Glu	Leu	Val
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Met Asp	Ser 1090 Ser	1079 Phe ) Gly	Gln Ile	Gly Leu Asp	Ile Arg 1110 Glu	Arg 1095 Pro	1080 Gln Ser	Pro Thr	Val Val Arg	Thr Asn 1115 Ile	Val 1100 Glu	1089 Thr Leu	Glu Glu	Leu Ser Leu	Val Gly 112 Gln
Met Asp 1105 Gln	Ser 1090 Ser Ile	Phe O Gly Ser	Gln Ile Tyr	Gly Leu Asp 1125	Ile Arg 1110 Glu	Arg 1099 Pro Val	1080 Gln Ser Gly	Pro Thr Glu	Val Val Arg	Thr Asn 1115 Ile	Val 1100 Glu Lys	1089 Thr Leu Asp	Glu Glu Glu Phe	Leu Ser Leu	Val Gly 112 Gln
Met Asp 1105 Gln	Ser 1090 Ser Ile	Phe O Gly Ser	Gln Ile Tyr	Gly Leu Asp 1125 Ile	Ile Arg 1110 Glu	Arg 1099 Pro Val	1080 Gln Ser Gly	Pro Thr Glu	Val Val Arg 1130 Asn	Thr Asn 1115 Ile	Val 1100 Glu Lys	1089 Thr Leu Asp	Glu Glu Glu Phe Lys	Leu Ser Leu 1135 Gln	Val Gly 112 Gln
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Met Asp 1105 Gln Gly Leu Ala Pro 1185 Leu Val Gln Leu	Ser 1090 Ser Ile Ser Gly Leu 1170 Val Val Thr Ala Glu 1250	Phe Gly Ser Ile 1155 Glu Ser Gly Gly Met 1235 Ala	Gln  Ile  Tyr  Cys 1140  Tyr  Leu  Asn  Ile  Tyr  1220  Asn  Gln	Asp 1125 Ile Glu Leu Leu Leu Lys Lys	Arg 1110 Glu Ala Ala Glu Arg 1190 Phe Asp Glu Ala	Arg 1099 Pro Val Gly Met Ala 1175 Leu Lys Pro Leu Thr	Gln Ser Gly Ile Lys 1160 Gln Pro Glu Glu Ile 1240 Gly	Pro Thr Glu Tyr 1145 Ile Ala Val Lys Thr 1225 Glu Gly	Val Val Arg 1130 Asn Gly Ala Glu Leu 1210 Gly Lys Ile	Asn Ille Glu Leu Thr Glu 1195 Leu Asn Gly Ile	Val 1100 Glu Lys Thr Val Gly 1180 Ala Ser Ile His Asp	Thr Leu Asp Thr Arg 1165 Phe Tyr Ala Ile Gly 1245 Pro	Glu Glu Phe Lys 1150 Pro Ile Lys Glu Ser 1230 Ile Lys	Leu Ser Leu 1135 Gln Gly Val Arg 1215 Leu Arg Glu	Val Gly 112 Gln Lys Thr Asp Gly 120 Ala Phe Leu Ser
Met Asp 1105 Gln Gly Leu Ala Pro 1185 Leu Val Gln Leu His	Ser 1090 Ser Ile Ser Gly Leu 1170 Val Thr Ala Glu 1250 Arg	Phe Gly Ser Ile 1155 Glu Ser Gly Gly Met 1235 Ala Leu	Gln Ile Tyr Cys 1140 Tyr Leu Asn Ile Tyr 1220 Asn Gln Pro	Leu Asp 1125 Ile Glu Leu Leu Glu 1205 Asn Lys Ile Val	Arg 1110 Glu Ala Ala Glu Arg 1190 Phe Asp Glu Ala Asp 1270	Arg 1099 Pro Val Gly Met Ala 1175 Leu Lys Pro Leu Thr 1255 Ile	Glu Glu Glu Glu Glu Glu Ala	Pro Thr Glu Tyr 1145 Ile Ala Val Lys Thr 1225 Glu Gly Tyr	Val Val Arg 1130 Asn Gly Ala Glu 1210 Gly Lys Ile Lys	Asn Ille Glu Leu Thr Glu 1195 Leu Asn Gly Ile Arg	Val 1100 Glu Lys Thr Val Gly 1180 Ala Ser Ile His Asp 1260 Gly	Thr Leu Asp Thr Arg 1165 Phe Tyr Ala Ile Gly 1245 Pro	Glu Glu Phe Lys 1150 Pro Ile Lys Glu Ser 1230 Ile Lys	Leu Ser Leu 1135 Gly Val Arg 1215 Leu Arg Glu Asn	Val Gly 112 Gln Lys Thr Asp Gly 120 Ala Phe Leu Ser Glu 128

			128	5				129	0				129	\ <b>r</b>
Phe Asp	Pro	Asn	Thr	Glu	Glu	Asn	Leu			Leu	Gln	Leu	Lvs	ro : Glu
		130	0				130	5				131	0	
Arg Cys	: Ile	Lys	Asp	Glu	Glu	Thr	Gly	Leu	Cys	Ļeu	Leu	Pro	Leu	Lys
	131	5				132	0				132	5		
Glu Lys	Lys	Lys	Gln	Val			Ser	Gln	Lys	Asn	Thr	Leu	Arg	Lys
133		<b>-</b>		_	133					134	0			-
Arg Arg	y Val	Val	Ile			Pro	Glu	Thr			Glu	Met	Ser	Val
1345	. 37.	M	7	135		_		_	135					136
Gln Glu	и Ата	Tyr	ьуs 136	г	GLY	Leu	ITE			Glu	Thr	Phe		
Len Cve	: (2) :	Gl n			G3.1	There	a1	137		m)	~-		137	5
Leu Cys	, OIu	138	n n	Cys	GIU	ııp	138		TTE	Thr	ite		_	Ser
Asp Gly	Ser			Val	Val	T.en			7~~	Tua	Th.	139	0 	<b>6</b> 3
	139	5	9			140		ДСР	Arg	цуs	140		ser	Gin
Tyr Asr	Ile	Gln	Asp	Ala	Ile			Glv	Leu	Val	Asn	o Ara	Laze	Pho
141	.0		_		141			1		142		****9	цуз	FIIG
Phe Asp	Gln	Tyr	Arg	Ser	Gly	Ser	Leu	Ser	Leu	Thr	Gln	Phe	Ala	Asn
1425				143	0				143	5				144
Met Ile	Ser	Leu	Lys	Asn	Gly	Val	Gly	Thr	Ser	Ser	Ser	Met	Gly	Ser
			144	5				145	0				145	5
Gly Val	Ser	qeA	Asp	Val	Phe	Ser	Ser	Ser	Arg	His	Glu	Ser	Val	Ser
I Tl.	0	1460		_	_		146	5				147	0	
Lys Ile	ser	Thr	IIe	Ser	Ser	Val	Arg	Asn	Leu	Thr	Ile	Arg	Ser	Ser
Ser Dhe	1475		mb.~	T	<b>~1</b>	1480		_	_		148	5		
Ser Phe	u per	Asp	Thr	Leu	149		ser	Ser	Pro			Ala	Ile	Phe
Asp Thr		Asn	T.e.ii	Glu			Sar	T1.0	mb w	1500	01	<b>+1</b> .	~1	_
1505				1510	בעם ז	116	Ser	116	151!		GLY	тте	GIu	_
Gly Ile	Val	asp	Ser			Glv	Gln	Ara	Len	T.011	Gl 11	7.1.	<i>α</i> 1	152
		-	1525	5		1		1530		Lcu	Gru	лта	153	
Cys Thr	Gly	Gly	Ile	Ile	His	Pro	Thr	Thr	Gly	Gln	Lvs	Leu	Ser	Leu
		1540	)				1545	;				1550	)	
Gln Asp	Ala	Val	Ser	Gln	Gly	Val	Ile	Asp	Gln	Asp	Met	Ala	Thr	Ser
	1555	,				1560	)				1569	5		
Val Lys	Pro	Ala	Gln	Lys	Ala	Phe	Ile	Gly	Phe	Glu	Gly	Val	Lys	Gly
157		<b></b> .	<b>a</b>		1579					1580	)			
Lys Lys 1585	пув	Mec	ser	1590	'Ата	GLu	Ala	Val			Lys	Trp	Leu	Pro
	Δ7 a	Gl v	Gln			T 011	<b>C1</b>	<b>15</b> -	1595	-	_			160
Tyr Glu	******	- x y	1605	Arg	FIIG	⊔eu	ътu	Pne 1610	GTU	ryr	ьeu	Thr		
Leu Val	Asp					Glv	Ara	TIA	Ser	ጥኮሎ	Gl.	C1	1619	71.
	•	1620	1			,	1625		Jer	1111	Giu	1630		TTE
Arg Lys	Gly	Phe	Ile	Asp	Gly	Arg			Gln	Arg	Leu	Gln	Asn	Thr
	1635					1640	l				1645	;		
Ser Ser	Tyr	Ala	Lys	Ile	Leu	Thr	Cys	Pro	Lys	Thr	Lys	Leu	Lvs	Ile
165	0				1655	5				1660	1			
Ser Tyr	Lys	qaA	Ala	Ile	Asn	Arg	Ser	Met	Val	Glu	Asp	Ile	Thr	Gly
1665				1670	)				1675					168
Leu Arg	Leu	Leu	Glu	Ala	Ala	Ser	Val	Ser	Ser	Lys	Gly	Leu	Pro	Ser
Dro m	7 ·		1685		<b>.</b> .	_		1690	l _				1695	
Pro Tyr	ASI	1190 1200	ser	ser	А1а	Pro	GLY	Ser	Arg	Ser	Gly			Ser
Glv Ser		1700 Ser		Sa~	λ~~		1705	0	<b>3</b>	0 -	~-3	1710	_	
Gly Ser	1715		O+ A	PET	Arg	5er 1720	атА	ser	arg				Arg	Arg
						1/20					1725			

Gly Ser Phe Asp Ala Thr Gly Asn Ser Ser Tyr Ser Tyr Ser Tyr Ser 1730 1735 Phe Ser Ser Ser Ile Gly His 1750 <210> 73 <211> 1978 <212> PRT <213> Homo Sapiens <400> 73 Met Ser Arg Pro Arg Phe Asn Pro Arg Gly Asp Phe Pro Leu Gln Arg Pro Arg Ala Pro Asn Pro Ser Gly Met Arg Pro Pro Gly Pro Phe Met 25 Arg Pro Gly Ser Met Gly Leu Pro Arg Phe Tyr Pro Ala Gly Arg Ala 40 Arg Gly Ile Pro His Arg Phe Ala Gly Leu Glu Ser Tyr Gln Asn Met Gly Pro Gln Arg Met Asn Val Gln Val Thr Gln His Arg Thr Asp Pro 75 Arg Leu Thr Lys Glu Lys Leu Asp Phe His Glu Ala Gln Gln Lys Lys 90 Gly Lys Pro His Gly Ser Arg Trp Asp Asp Glu Pro His Ile Ser Ala 105 Ser Val Ala Val Lys Gln Ser Ser Val Thr Gln Val Thr Glu Gln Ser 120 125 Pro Lys Val Gln Ser Arg Tyr Thr Lys Glu Ser Ala Ser Ser Ile Leu 135 Ala Ser Phe Gly Leu Ser Asn Glu Asp Leu Glu Glu Leu Ser Arg Tyr 150 155 Pro Asp Glu Gln Leu Thr Pro Glu Asn Met Pro Leu Ile Leu Arg Asp 165 170 175 Ile Arg Met Arg Lys Met Gly Arg Arg Leu Pro Asn Leu Pro Ser Gln 185 190 Ser Arg Asn Lys Glu Thr Leu Gly Ser Glu Ala Val Ser Ser Asn Val 200 Ile Asp Tyr Gly His Ala Ser Lys Tyr Gly Tyr Thr Glu Asp Pro Leu 215 220 Glu Val Arg Ile Tyr Asp Pro Glu Ile Pro Thr Asp Glu Val Glu Asn 235 Glu Phe Gln Ser Gln Gln Asn Ile Ser Ala Ser Val Pro Asn Pro Asn 245 250 Val Ile Cys Asn Ser Met Phe Pro Val Glu Asp Val Phe Arg Gln Met

Phe Ser Ser Glu Leu Ile Ser Ser Val Ser Gln Gln Glu Arg Ile Pro 340 345 350

His Glu Pro Val Ile Asn Ser Ser Asn Val His Val Gly Ser Arg Gly 360 Ser Lys Lys Asn Tyr Gln Ser Gln Ala Asp Ile Pro Ile Arg Ser Pro 375 Phe Gly Ile Val Lys Ala Ser Trp Leu Pro Lys Phe Ser His Ala Asp 390 395 Ala Gln Lys Met Lys Arg Leu Pro Thr Pro Ser Met Met Asn Asp Tyr 405 410 Tyr Ala Ala Ser Pro Arg Ile Phe Pro His Leu Cys Ser Leu Cys Asn 425 Val Glu Cys Ser His Leu Lys Asp Trp Ile Gln His Gln Asn Thr Ser 440 Thr His Ile Glu Ser Cys Arg Gln Leu Arg Gln Gln Tyr Pro Asp Trp 455 Asn Pro Glu Ile Leu Pro Ser Arg Arg Asn Glu Gly Asn Arg Lys Glu 470 475 Asn Glu Thr Pro Arg Arg Ser His Ser Pro Ser Pro Arg Arg Ser 485 490 Arg Arg Ser Ser Ser His Arg Phe Arg Arg Ser Arg Ser Pro Met 500 505 His Tyr Met Tyr Arg Pro Arg Ser Arg Ser Pro Arg Ile Cys His Arg 520 525 Phe Ile Ser Arg Tyr Arg Ser Arg Ser Arg Ser Arg Ser Pro Tyr Arg 535 540 Ile Arg Asn Pro Phe Arg Gly Ser Pro Lys Cys Phe Arg Ser Val Ser 550 555 Pro Glu Arg Met Ser Arg Arg Ser Val Arg Ser Ser Asp Arg Lys Lys 565 570 Ala Leu Glu Asp Val Val Gln Arg Ser Gly His Gly Thr Glu Phe Asn 585 Lys Gln Lys His Leu Glu Ala Ala Asp Lys Gly His Ser Pro Ala Gln 600 Lys Pro Lys Thr Ser Ser Gly Thr Lys Pro Ser Val Lys Pro Thr Ser 615 620 Ala Thr Lys Ser Asp Ser Asn Leu Gly Gly His Ser Ile Arg Cys Lys 630 635 Ser Lys Asn Leu Glu Asp Asp Thr Leu Ser Glu Cys Lys Gln Val Ser 645 650 Asp Lys Ala Val Ser Leu Gln Arg Lys Leu Arg Lys Glu Gln Ser Leu 660 665 His Tyr Gly Ser Val Leu Leu Ile Thr Glu Leu Pro Glu Asp Gly Cys 680 Thr Glu Glu Asp Val Arg Lys Leu Phe Gln Pro Phe Gly Lys Val Asn 695 Asp Val Leu Ile Val Pro Tyr Arg Lys Glu Ala Tyr Leu Glu Met Glu 710 715 Phe Lys Glu Ala Ile Thr Ala Ile Met Lys Tyr Ile Glu Thr Thr Pro 730 Leu Thr Ile Lys Gly Lys Ser Val Lys Ile Cys Val Pro Gly Lys Lys 745 Lys Ala Gln Asn Lys Glu Val Lys Lys Lys Thr Leu Glu Ser Lys Lys 760 Val Ser Ala Ser Thr Leu Lys Arg Asp Ala Asp Ala Ser Lys Ala Val 775 Glu Ile Val Thr Ser Thr Ser Ala Ala Lys Thr Gly Gln Ala Lys Ala

785				790					705					
Cys Val	בומ	Larg	Va 1		Larg	Sar	mh~	C111	795	Com	77.	0		800
cys var	7114		805	71011	<b></b> y5	Der	1111	810	пур	per	ATG	ser		vai
Lys Ser	V=1	Va l		1727	ב [ ג	77-1	Tare		200	T	7.7.	0	815	
nys ser	Val	820	1111	Val	нта	val	825	GIY	ASII	'nλ≳	Ala		тте	гÀг
Thr Ala	Tare		Gl v	Clv	Taro	Tara		T 011	<i>α</i> 3	71-	*	830	m)	~3
IIII AIG	835	261	GIY	Gry	цуs		Ser	Leu	GIU	Ala		гуѕ	Thr	GTA
Acn Wal		N c m	T 110	7	C	840	T	<b>D</b>	**- 1		845	_		_
Asn Val 850	пур	ASII	пåя	Asp		ASI	гÀг	Pro	vaı		тте	Pro	GLu	Asn
	Tlo	Tura	Πp ≈	Com	855	<b>a</b> 3	17 7	<b>.</b>	77-	860	~1	_	_	_ •
Ser Glu 865	116	гуз	1111		TTE	GIU	vaı	гÀг		Thr	GIU	Asn	Cys	
	~ דת	Tlo	602	870	71.	77-	T	<b>~1</b>	875	<b></b> 1	~1	_		880
Lys Glu	Ата	116		Asp	Ala	Ата	Leu		Ата	Thr	GLu	Asn		Pro
Leu Asp	Larg	C1	885	C1	<b>01</b>	Mob	<b></b>	890	W- L	<b>.</b> .		_	895	_
Leu Asn	ьys		THE	GIU	GIU	Mec		vaı	мес	Leu	val		Asn	Leu
Dro Agn	7	900	(T)		**- 7	<b>~</b> 3	905	•••	_	_	_	910		
Pro Asn	ьуs 915	GIY	туг	ser	vaı		GIU	val	Tyr	Asp		Ala	Lys	Pro
nha al	-	T	<b>7</b>	3	<b>~</b> 1 -	920		_	_	_	925			
Phe Gly 930	GIY	Leu	гуs	Asp		Leu	ITe	Leu	Ser		His	Lys	Lys	Ala
	<b>01</b>	T1 -	<b>3</b>	•	935					940				
Tyr Ile	GIU	TTG	Asn		ьуѕ	Ala	Ala	Glu		Met	Val	Lys	Phe	Tyr
945	Dh.a	5	**- 7	950		_		_	955					960
Thr Cys	Pne	Pro		Leu	Met	Asp	GIY		Gln	Leu	Ser	Ile		Met
Ala Dwa	<b>~</b> 1	<b>3</b>	965	<b>.</b>	~7 -	_	_	970		_ ~			975	
Ala Pro	GIU		Met	Asn	TTE	ьys		GIu	GIu	Ala	Ile		Ile	Thr
Ton 1751	T	980	3	7	D	<b>~</b> 1	985	_		_		990		
Leu Val		GIU	Asn	Asp	Pro			Asn	He	Asp			Tyr	Asp
Awa Dha	995	TT-:	<b>7</b>	*	3	1000		~-7	_		1005			
Arg Phe		HIS	Leu	Asp			Pro	GIU	Asp			Gln	Cys	Val
		<b>~1</b>	T	<b>~1</b>	1019				_	1020				_
Leu Cys 1025	vaı	GIA	Leu			GIY	ьуs	vaı			His	Val	Phe	
	7~~	7 ~~	T	1030		T	<b>~</b> 3	<b>.</b>	1035		_		_	104
Ser Asn	Ary	ASII			TTG	Leu	GIN			ser	Pro	GIu		
Cln Con	Mot	M	1045		T	*	<b>~</b> 3	1050			_		1055	
Gln Ser	Mec			Pne	ьеи	ьуs			Pro	GIn	Asn		_	Asp
III - Mah	<b>T</b>	1060			-		1065			_		1070		
His Met			Cys	ser	Leu			Lys	Ile	Asp			Glu	Val
Clm Tla	1079		2	D	<b>~</b> 1	1080		_		_	1085			
Gln Ile		HIS	Asp	Pro			GIU	гàг	GLu			Gly	Leu	Lys
1090		T1.	3	<b>a</b> 3	1095			~-		1100				
Asn Ser	Pro					GLu	Val				Thr	Asp	Ser	Pro
1105	<b>+</b>		•			~-3			1115					112
Ser Val	гуѕ	Pro			Leu	GLu	GIu			Thr	Pro	Ser		
mb Gl	m1	<b>.</b>	1125		~-1			1130					1135	
Thr Glu	Thr			GIn	GIn				Cys	Glu	Glu			Glu
	m1	1140		_	_		1145		_	_		1150		
Lys Ala			Asp	Ser	Asp			Val	Glu	Thr			Leu	Glu
m1: ~3	1159				_	1160					1165			
Thr Gln		GIu	GLu	Val			Glu	Ile	Pro			Ala	Ser	Ala
1170					1175					1180				
	_		~1	Gln	Phe	Thr	Glu	Asn	Ala		Glu	Cys	Ala	Leu
Ser Val	Ser	TTE	GIU											
Ser Val 1185				1190	)				1195					120
Ser Val			Phe	1190 <b>A</b> sn	)		Leu		Lys		Gly	Ala		
Ser Val 1185 Asn Gln	Gln	Met	Phe 1205	1190 Asn	Ser	Asp		1210	Lys	Lys			Glu 1215	Ile
Ser Val 1185	Gln	Met	Phe 1205 Thr	1190 Asn	Ser	Asp		1210 Ser	Lys	Lys			Glu 1215	Ile

Glu Arg Asn Leu Lys Gly Ile Leu Glu Glu Ser Pro Ser Glu Ala Glu 1235 1240 Asp Phe Ile Ser Gly Ile Thr Gln Thr Met Val Glu Ala Val Ala Glu 1255 Val Glu Lys Asn Glu Thr Val Ser Glu Ile Leu Pro Ser Thr Cys Ile 1270 1275 128 Val Thr Leu Val Pro Gly Ile Pro Thr Gly Asp Glu Lys Thr Val Asp 1285 1290 1295 Lys Lys Asn Ile Ser Glu Lys Lys Gly Asn Met Asp Glu Lys Glu Glu 1300 1305 Lys Glu Phe Asn Thr Lys Glu Thr Arg Met Asp Leu Gln Ile Gly Thr 1315 1320 Glu Lys Ala Glu Lys Asn Glu Gly Arg Met Asp Ala Glu Lys Val Glu 1330 1335 1340 Lys Met Ala Ala Met Lys Glu Lys Pro Ala Glu Asn Thr Leu Phe Lys 1350 1355 Ala Tyr Pro Asn Lys Gly Val Gly Gln Ala Asn Lys Pro Asp Glu Thr 1365 1370 Ser Lys Thr Ser Ile Leu Ala Val Ser Asp Val Ser Ser Ser Lys Pro 1385 1390 Ser Ile Lys Ala Val Ile Val Ser Ser Pro Lys Ala Lys Ala Thr Val 1400 Ser Lys Thr Glu Asn Gln Lys Ser Phe Pro Lys Ser Val Pro Arg Asp 1415 1420 Gln Ile Asn Ala Glu Lys Lys Leu Ser Ala Lys Glu Phe Gly Leu Leu 1430 1435 Lys Pro Thr Ser Ala Arg Ser Gly Leu Ala Glu Ser Ser Ser Lys Phe 1445 1450 1455 Lys Pro Thr Gln Ser Ser Leu Thr Arg Gly Gly Ser Gly Arg Ile Ser 1460 1465 1470 Ala Leu Gln Gly Lys Leu Ser Lys Leu Asp Tyr Arg Asp Ile Thr Lys 1475 1480 1485 Gln Ser Gln Glu Thr Glu Ala Arg Pro Ser Ile Met Lys Arg Asp Asp 1490 1495 1500 Ser Asn Asn Lys Thr Leu Ala Glu Gln Asn Thr Lys Asn Pro Lys Ser 1505 1510 1515 152 Thr Thr Gly Arg Ser Ser Lys Ser Lys Glu Glu Pro Leu Phe Pro Phe 1525 1530 Asn Leu Asp Glu Phe Val Thr Val Asp Glu Val Ile Glu Glu Val Asn 1540 1545 1550 Pro Ser Gln Ala Lys Gln Asn Pro Leu Lys Gly Lys Arg Lys Glu Thr 1560 Leu Lys Asn Val Pro Phe Ser Glu Leu Asn Leu Lys Lys Lys Gly 1575 1580 Lys Thr Ser Thr Pro Arg Gly Val Glu Gly Glu Leu Ser Phe Val Thr 1590 1595 Leu Asp Glu Ile Gly Glu Glu Asp Ala Ala His Leu Ala Gln 1605 1610 Ala Leu Val Thr Val Asp Glu Val Ile Asp Glu Glu Leu Asn Met 1625 Glu Glu Met Val Lys Asn Ser Asn Ser Leu Phe Thr Leu Asp Glu Leu 1640 1645 Ile Asp Gln Asp Asp Cys Ile Ser His Ser Glu Pro Lys Asp Val Thr 1655 1660 Val Leu Ser Val Ala Glu Glu Gln Asp Leu Leu Lys Gln Glu Arg Leu

1665 1670 1675 Val Thr Val Asp Glu Ile Gly Glu Val Glu Glu Leu Pro Leu Asn Glu 1690 Ser Ala Asp Ile Thr Phe Ala Thr Leu Asn Thr Lys Gly Asn Glu Gly 1705 Asp Ile Val Arg Asp Ser Ile Gly Phe Ile Ser Ser Gln Val Pro Glu 1715 1720 1725 Asp Pro Ser Thr Leu Val Thr Val Asp Glu Ile Gln Asp Asp Ser Ser 1735 1740 Asp Leu His Leu Val Thr Leu Asp Glu Val Thr Glu Glu Asp Glu Asp 1750 1755 Ser Leu Ala Asp Phe Asn Asn Leu Lys Glu Glu Leu Asn Phe Val Thr 1765 1770 Val Asp Glu Val Gly Glu Glu Asp Gly Asp Asn Asp Leu Lys Val 1780 1785 Glu Leu Ala Gln Ser Lys Asn Asp His Pro Thr Asp Lys Lys Gly Asn 1800 1805 Arg Lys Lys Arg Ala Val Asp Thr Lys Lys Thr Lys Leu Glu Ser Leu 1815 1820 Ser Gln Val Gly Pro Val Asn Glu Asn Val Met Glu Glu Asp Leu Lys 1830 1835 Thr Met Ile Glu Arg His Leu Thr Ala Lys Thr Pro Thr Lys Arg Val 1845 1850 Arg Ile Gly Lys Thr Leu Pro Ser Glu Lys Ala Val Val Thr Glu Pro 1860 1865 Ala Lys Gly Glu Glu Ala Phe Gln Met Ser Glu Val Asp Glu Glu Ser 1880 Gly Leu Lys Asp Ser Glu Pro Glu Arg Lys Arg Lys Lys Thr Glu Asp 1895 1900 Ser Ser Ser Gly Lys Ser Val Ala Ser Asp Val Pro Glu Glu Leu Asp 1910 1915 Phe Leu Val Pro Lys Ala Gly Phe Phe Cys Pro Ile Cys Ser Leu Phe 1925 1930 1935 Tyr Ser Gly Glu Lys Ala Met Thr Asn His Cys Lys Ser Thr Arg His 1940 1945 Lys Gln Asn Thr Glu Lys Phe Met Ala Lys Gln Arg Lys Glu Lys Glu 1955 1960 Gln Asn Glu Ala Glu Glu Arg Ser Ser Arg 1970 1975 <210> 74 <211> 366 <212> PRT <213> Homo Sapiens <400> 74 Met Arg Val Met Ala Pro Arg Thr Leu Ile Leu Leu Ser Gly Ala 1 10 Leu Ala Leu Thr Glu Thr Trp Ala Gly Ser His Ser Met Arg Tyr Phe 20 Tyr Thr Ala Val Ser Arg Pro Gly Arg Gly Glu Pro His Phe Ile Ala 40 Val Gly Tyr Val Asp Asp Thr Gln Phe Val Arg Phe Asp Ser Asp Ala 55

Ala Ser Pro Arg Gly Glu Pro Arg Ala Pro Trp Val Glu Gln Glu Gly

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65
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Pro Glu Tyr Trp Asp Arg Glu Thr Gln Lys Tyr Lys Arg Gln Ala Gln
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Thr Asp Arg Val Ser Leu Arg Asn Leu Arg Gly Tyr Tyr Asn Gln Ser
                               105
Glu Ala Gly Ser His Ile Ile Gln Arg Met Tyr Gly Cys Asp Val Gly
                           120
Pro Asp Gly Arg Leu Leu Arg Gly Tyr Asp Gln Tyr Ala Tyr Asp Gly
                        135
                                           140
Lys Asp Tyr Ile Ala Leu Asn Glu Asp Leu Arg Ser Trp Thr Ala Ala
                   150
                                       155
Asp Thr Ala Ala Gln Ile Thr Gln Arg Lys Trp Glu Ala Ala Arg Glu
               165
                                    170
Ala Glu Gln Leu Arg Ala Tyr Leu Glu Gly Leu Cys Val Glu Trp Leu
                                185
Arg Arg Tyr Leu Lys Asn Gly Lys Glu Thr Leu Gln Arg Ala Glu His
                            200
Pro Lys Thr His Val Thr His His Pro Val Ser Asp His Glu Ala Thr
                        215
Leu Arg Cys Trp Ala Leu Gly Phe Tyr Pro Ala Glu Ile Thr Leu Thr
                                       235
Trp Gln Trp Asp Gly Glu Asp Gln Thr Gln Asp Thr Glu Leu Val Glu
                245
                                   250
Thr Arg Pro Ala Gly Asp Gly Thr Phe Gln Lys Trp Ala Ala Val Val
                               265
Val Pro Ser Gly Glu Glu Gln Arg Tyr Thr Cys His Val Gln His Glu
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Gly Leu Pro Glu Pro Leu Thr Leu Arg Trp Glu Pro Ser Ser Gln Pro
                       295
Thr Ile Pro Ile Val Gly Ile Val Ala Gly Leu Ala Val Leu Ala Val
                    310
                                       315
Leu Ala Val Leu Gly Ala Val Val Ala Val Val Met Cys Arg Arg Lys
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                                   330
Ser Ser Gly Gly Lys Gly Gly Ser Cys Ser Gln Ala Ala Ser Ser Asn
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Ser Ala Gln Gly Ser Asp Glu Ser Leu Ile Ala Cys Lys Ala
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                           360
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Val Tyr Ile Phe Ala Lys Lys Asn Asp Ile Pro Phe Glu Leu Arg Ile
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Thr Glu Ser Val Ala Ile Leu Leu Tyr Leu Thr Arg Lys Tyr Lys Val Pro Asp Tyr Trp Tyr Pro Gln Asp Leu Gln Ala Arg Ala Arg Val Asp

Val Asp Leu Ile Lys Gly Gln His Leu Ser Asp Ala Phe Ala Gln Val

Asn Pro Leu Lys Lys Val Pro Ala Leu Lys Asp Gly Asp Phe Thr Leu

55

85 90 Glu Tyr Leu Ala Trp Gln His Thr Thr Leu Arg Arg Ser Cys Leu Arg 100 105 Ala Leu Trp His Lys Val Met Phe Pro Val Phe Leu Gly Gly Pro Val 120 125 Ser Pro Gln Thr Leu Ala Ala Thr Leu Ala Glu Leu Asp Val Thr Leu 135 Gln Leu Leu Glu Asp Lys Phe Leu Gln Asn Lys Ala Phe Leu Thr Gly 150 155 Pro His Ile Ser Leu Ala Asp Leu Val Ala Ile Thr Glu Leu Met His 170 Pro Val Gly Ala Gly Cys Gln Val Phe Glu Gly Arg Pro Lys Leu Ala 185 Thr Trp Arg Gln Arg Val Glu Ala Ala Val Gly Glu Asp Leu Phe Gln Glu Ala His Glu Val Ile Leu Lys Ala Lys Asp Phe Pro Pro Ala Asp 215 Pro Thr Ile Lys Gln Lys Leu Met Pro Trp Val Leu Ala Met Ile Arg 230 235 <210> 76 <211> 953 <212> PRT <213> Homo Sapiens

<400> 76

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225					230					235					240
Asn	Leu	Leu	Met	Ala 245	Tyr	Gln	Ile	Cys	Phe 250	Asp		Tyr	Glu	Ser 255	Ala
			260					265					270	Val	Gly
Thr	Pro	Ile 275	Ala	Ser	Val	Pro	Gly 280		Thr	Asn	Thr	Gly 285		Val	Pro
	290					295					300				Ser
305					310					315					Asp 320
				325					330					335	
			340					345		Asn			350		
		355					360			Ser		365			
	370					375				Gly	380				
385					390					Arg 395					400
				405					410				_	415	
			420					425		Leu			430		
		435					440			Leu		445			
	450					455				Asp	460				
465					470					His 475					480
				485					490	Gln				495	
			500					505		Val			510		
		<b>51</b> 5					520			Ser		525			
	530					<b>5</b> 35				Thr	540				
545					550					Val 555					560
				565					570	Cys				575	
			580					585		Ala			590		
		595					600			Leu		605			
	610					615				Val	620				
625					630					Ser 635					640
				645					650	Gly				655	
GTÀ	тте	Cys	Cys 660	Ala	Gly	Thr	Gly	Asn 665	Lys	Glu	Ala	Ile	Asn 670	Leu	Leu

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Glu Pro Met Thr Asn Asp Pro Val Asn Tyr Val Arg Gln Gly Ala Leu
                680
Ile Ala Ser Ala Leu Ile Met Ile Gln Gln Thr Glu Ile Thr Cys Pro
             . 695
Lys Val Asn Gln Phe Arg Gln Leu Tyr Ser Lys Val Ile Asn Asp Lys
                  710
                                      715
His Asp Asp Val Met Ala Lys Phe Gly Ala Ile Leu Ala Gln Gly Ile
               725
                                   730
Leu Asp Ala Gly Gly His Asn Val Thr Ile Ser Leu Gln Ser Arg Thr
           740
                              745
Gly His Thr His Met Pro Ser Val Val Gly Val Leu Val Phe Thr Gln
                          760
Phe Trp Phe Trp Phe Pro Leu Ser His Phe Leu Ser Leu Ala Tyr Thr
                       775
                                          780
Pro Thr Cys Val Ile Gly Leu Asn Lys Asp Leu Lys Met Pro Lys Val
                   790
                                      795
Gln Tyr Lys Ser Asn Cys Lys Pro Ser Thr Phe Ala Tyr Pro Ala Pro
                                   810
Leu Glu Val Pro Lys Glu Lys Glu Lys Glu Lys Val Ser Thr Ala Val
           820
Leu Ser Ile Thr Ala Lys Ala Lys Lys Lys Glu Lys Glu Lys Glu Lys
                           840
Lys Glu Glu Lys Met Glu Val Asp Glu Ala Glu Lys Lys Glu Glu
                       855
                                          860
Lys Glu Lys Lys Glu Pro Glu Pro Asn Phe Gln Leu Leu Asp Asn
                  870
                                     875
Pro Ala Arg Val Met Pro Ala Gln Leu Lys Val Leu Thr Met Pro Glu
              885
                                 890
Thr Cys Arg Tyr Gln Pro Phe Lys Pro Leu Ser Ile Gly Gly Ile Ile
          900
                              905
Ile Leu Lys Asp Thr Ser Glu Asp Ile Glu Glu Leu Val Glu Pro Val
                          920
Ala Ala His Gly Pro Lys Ile Glu Glu Glu Glu Gln Glu Pro Glu Pro
                     935
                                          940
Pro Glu Pro Phe Glu Tyr Ile Asp Asp
945
                   950
     <210> 77
     <211> 335
     <212> PRT
     <213> Homo Sapiens
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<400> 77

 Met
 Gly
 Lys
 Val
 Lys
 Val
 Gly
 Val
 Asn
 Gly
 Phe
 Gly
 Arg
 Leg
 Arg
 Ala
 Ala
 Phe
 Asn
 Ser
 Gly
 Lys
 Val
 Asp
 Ile
 Val
 Ala

 Leu
 Asn
 Est
 Tyr
 Met
 Val
 Tyr
 Met
 Phe
 Gln
 Asn
 Asn
 Tyr
 Met
 Val
 Tyr
 Met
 Phe
 Gln
 Asn
 ```
Glu Ser Thr Gly Val Phe Thr Thr Met Glu Lys Ala Gly Ala His Leu
           100
Gln Gly Gly Ala Lys Arg Val Ile Ile Ser Ala Pro Ser Ala Asp Ala
                           120
Pro Met Phe Val Met Gly Val Asn His Glu Lys Tyr Asp Asn Ser Leu
                      135
Lys Ile Ile Ser Asn Ala Ser Cys Thr Thr Asn Cys Leu Ala Pro Leu
                  150
                                       155
Ala Lys Val Ile His Asp Asn Phe Gly Ile Val Glu Gly Leu Met Thr
               165
                                   170
Thr Val His Ala Ile Thr Ala Thr Gln Lys Thr Val Asp Gly Pro Ser
           180
                              185
Gly Lys Leu Trp Arg Asp Gly Arg Gly Ala Leu Gln Asn Ile Ile Pro
                          200
Ala Ser Thr Gly Ala Ala Lys Ala Val Gly Lys Val Ile Pro Glu Leu
                       215
                                           220
Asn Gly Lys Leu Thr Gly Met Ala Phe Arg Val Pro Thr Ala Asn Val
                   230
                                       235
Ser Val Val Asp Leu Thr Cys Arg Leu Glu Lys Pro Ala Lys Tyr Asp
               245
                                   250
Asp Ile Lys Lys Val Val Lys Gln Ala Ser Glu Gly Pro Leu Lys Gly
                               265
Ile Leu Gly Tyr Thr Glu His Gln Val Val Ser Ser Asp Phe Asn Ser
                           280
Asp Thr His Ser Ser Thr Phe Asp Ala Gly Ala Gly Ile Ala Leu Asn
                      295
                                          300
Asp His Phe Val Lys Leu Ile Ser Trp Tyr Asp Asn Glu Phe Gly Tyr
                 310
                                      315
Ser Asn Arg Val Val Asp Leu Met Ala His Met Ala Ser Lys Glu
                                   330
     <210> 78
     <211> 117
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      <213> Homo Sapiens
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Met Val Gln Arg Leu Thr Tyr Arg Arg Arg Leu Ser Tyr Asn Thr Ala
                                   10
Ser Asn Lys Thr Arg Leu Ser Arg Thr Pro Gly Asn Arg Ile Val Tyr
          20
Leu Tyr Thr Lys Lys Val Gly Lys Ala Pro Lys Ser Ala Cys Gly Val
                           40
Cys Pro Gly Lys Leu Arg Gly Val Arg Pro Val Arg Pro Lys Val Leu
                       55
Met Arg Leu Ser Lys Thr Lys Lys His Val Ser Arg Ala Tyr Gly Gly
Ser Met Cys Ala Lys Cys Val Arg Asp Arg Ile Lys Arg Ala Phe Leu
                                  90
Ile Glu Glu Gln Lys Ile Ile Val Lys Val Leu Lys Ala Gln Ala Gln
           100
                             105
Ser Gln Lys Ala Lys
       115
```

<210> 79

<211> 614 <212> PRT <213> Homo Sapiens

<400> 79 Arg Ser Gly Gln Pro Arg Ala Glu Gly Leu Gly Ala Gly Ala Ala Gly Pro Leu Arg Ala Met Ala Ala Pro Val Lys Gly Asn Arg Lys Gln Ser Thr Glu Gly Asp Ala Leu Asp Pro Pro Ala Ser Pro Lys Pro Ala Gly 40 Lys Gln Asn Gly Ile Gln Asn Pro Ile Ser Leu Glu Asp Ser Pro Glu Ala Gly Gly Glu Arg Glu Glu Glu Glu Glu Arg Glu Glu Glu Gln Ala Phe Leu Val Ser Leu Tyr Lys Phe Met Lys Glu Arg His Thr Pro Ile 90 Glu Arg Val Pro His Leu Gly Phe Lys Gln Ile Asn Leu Trp Lys Ile 105 Tyr Lys Ala Val Glu Lys Leu Gly Ala Tyr Glu Leu Val Thr Gly Arg 120 Arg Leu Trp Lys Asn Val Tyr Asp Glu Leu Gly Gly Ser Pro Gly Ser 135 Thr Ser Ala Ala Thr Cys Thr Arg Arg His Tyr Glu Arg Leu Val Leu 150 155 Pro Tyr Val Arg His Leu Lys Gly Glu Asp Asp Lys Pro Leu Pro Thr 170 Ser Lys Pro Arg Lys Gln Tyr Lys Met Ala Lys Glu Asn Arg Gly Asp 180 185 Asp Gly Ala Thr Glu Arg Pro Lys Lys Ala Lys Glu Glu Arg Arg Met 200 Asp Gln Met Met Pro Gly Lys Thr Lys Ala Asp Ala Asp Pro Ala 215 220 Pro Leu Pro Ser Gln Glu Pro Pro Arg Asn Ser Thr Glu Gln Gly 235 230 Leu Ala Ser Gly Ser Ser Val Ser Phe Val Gly Ala Ser Gly Cys Pro 245 250 Glu Ala Tyr Lys Arg Leu Leu Ser Ser Phe Tyr Cys Lys Gly Thr His 265 Gly Ile Met Ser Pro Leu Ala Lys Lys Leu Leu Ala Gln Val Ser 280 Lys Val Glu Ala Leu Gln Cys Gln Glu Glu Gly Cys Arg His Gly Ala 295 300 Glu Pro Gln Ala Ser Pro Ala Val His Leu Pro Glu Ser Pro Gln Ser 310 315 Pro Lys Gly Leu Thr Glu Asn Ser Arg His Arg Leu Thr Pro Gln Glu 325 330 Gly Leu Gln Ala Pro Gly Gly Ser Leu Arg Glu Glu Ala Gln Ala Gly Pro Cys Pro Ala Ala Pro Ile Phe Lys Gly Cys Phe Tyr Thr His Pro 360 365 Thr Glu Val Leu Lys Pro Val Ser Gln His Pro Arg Asp Phe Phe Ser 375

Arg Leu Lys Asp Gly Val Leu Leu Gly Pro Pro Gly Lys Glu Gly Leu

380

```
Ser Val Lys Glu Pro Gln Leu Val Trp Gly Gly Asp Ala Asn Arg Pro
                405
                                  410
Ser Ala Phe His Lys Gly Gly Ser Arg Lys Gly Ile Leu Tyr Pro Lys
                               425
Pro Lys Ala Cys Trp Val Ser Pro Met Ala Lys Val Pro Ala Glu Ser
                           440
Pro Thr Leu Pro Pro Thr Phe Pro Ser Ser Pro Gly Leu Gly Ser Lys
                        455
                                           460
Arg Ser Leu Glu Glu Glu Gly Ala Ala His Ser Gly Lys Arg Leu Arg
                 470
                                       475
Ala Val Ser Pro Phe Leu Lys Glu Ala Asp Ala Lys Lys Cys Gly Ala
               485
                                   490
Lys Pro Ala Gly Ser Gly Leu Val Ser Cys Leu Leu Gly Pro Ala Leu
            500
                                505
Gly Pro Val Pro Pro Glu Ala Tyr Arg Gly Thr Met Leu His Cys Pro
                           520
Leu Asn Phe Thr Gly Thr Pro Gly Pro Leu Lys Gly Gln Ala Ala Leu
                        535
Pro Phe Ser Pro Leu Val Ile Pro Ala Phe Pro Ala His Phe Leu Ala
                   550
                                       555
Thr Ala Gly Pro Ser Pro Met Ala Ala Gly Leu Met His Phe Pro Pro
               565
                                   570
Thr Ser Phe Asp Ser Ala Leu Arg His Arg Leu Cys Pro Ala Ser Ser
                              585
Ala Trp His Ala Pro Pro Val Thr Thr Tyr Ala Ala Pro His Phe Phe
                          600
His Leu Asn Thr Lys Leu
    610
      <210> 80
      <211> 114
      <212> PRT
      <213> Homo Sapiens
     <400> 80
Met Ala Ser Val Ser Glu Leu Ala Cys Ile Tyr Ser Ala Leu Ile Leu
                                   10
His Asp Asp Glu Val Thr Val Thr Glu Asp Lys Ile Asn Ala Leu Ile
          20
                               25
Lys Ala Ala Gly Val Asn Val Glu Pro Phe Trp Pro Gly Leu Phe Ala
                           40
Lys Ala Leu Ala Asn Val Asn Ile Gly Ser Leu Ile Cys Asn Val Gly
Ala Gly Gly Pro Ala Pro Ala Ala Gly Ala Ala Pro Ala Gly Gly Pro
                   70
Ala Pro Ser Thr Ala Ala Pro Ala Glu Glu Lys Lys Val Glu Ala
Lys Lys Glu Glu Ser Glu Glu Ser Asp Asp Met Gly Phe Gly Leu
                               105
Phe Asp
     <210> 81
     <211> 596
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-52-

<212> PRT

## <213> Homo Sapiens

<400> 81 Met Arg Arg Ala His Glu Gly Arg Glu Ile Pro Ser Leu Gly Gly Ala 10 Arg Arg Arg Glu Val Leu Gln Ala Gly Arg Ser Gln Arg Ala Ala Gly 25 Arg Arg Arg Arg Gln Glu Leu Glu Leu Gly Val Gly Ser Gly Arg 40 Pro Gly Gly Pro Pro Pro Gly Pro Gly Arg Arg Gly Thr Cys Ala Ala 55 Ala Leu Pro Pro Glu Trp Pro Arg Arg Arg Thr Gly Leu Pro Arg Arg 70 75 Gly Pro Arg Pro Pro Leu Ala Met Ala Lys Trp Leu Asn Lys Tyr Phe 85 90 Ser Leu Gly Asn Ser Lys Thr Lys Ser Pro Pro Gln Pro Pro Arg Pro 105 Asp Tyr Arg Glu Gln Arg Arg Gly Glu Arg Pro Ser Gln Pro Pro 120 Gln Ala Val Pro Gln Ala Ser Ser Ala Ala Ser Ala Ser Cys Gly Pro 135 Ala Thr Ala Ser Cys Phe Ser Ala Ser Ser Gly Ser Leu Pro Asp Asp 155 Ser Gly Ser Thr Ser Asp Leu Ile Arg Ala Tyr Arg Ala Gln Lys Glu 170 Arg His Phe Gln Asp Pro Tyr Asn Gly Pro Gly Ser Ser Leu Arg Lys 185 Leu Arg Ala Met Cys Arg Leu Asp Tyr Cys Gly Gly Ser Gly Glu Pro 200 Gly Gly Val Gln Arg Ala Phe Ser Ala Ser Ser Ala Ser Gly Ala Ala 215 Gly Cys Cys Cys Ala Ser Ser Gly Ala Gly Ala Ala Ala Ser Ser Ser 230 235 Ser Ser Ser Gly Ser Pro His Leu Tyr Arg Ser Ser Ser Glu Arg Arg 245 250 Pro Ala Thr Pro Ala Glu Val Arg Tyr Ile Ser Pro Lys His Arg Leu 260 265 Ile Lys Val Glu Ser Ala Ala Gly Gly Gly Ala Gly Asp Pro Leu Gly 280 Gly Ala Cys Ala Gly Gly Arg Thr Trp Ser Pro Thr Ala Cys Gly Gly 295 300 Lys Lys Leu Leu Asn Lys Cys Ala Ala Ser Ala Ala Glu Glu Ser Gly 310 315 Ala Gly Lys Lys Asp Lys Val Thr Ile Ala Asp Asp Tyr Ser Asp Pro 330 Phe Asp Ala Lys Asn Asp Leu Lys Ser Lys Ala Gly Lys Gly Glu Ser 340 Ala Gly Tyr Met Glu Pro Tyr Glu Ala Gln Arg Ile Met Thr Glu Phe 360 Gln Arg Gln Glu Ser Val Arg Ser Gln His Lys Gly Ile Gln Leu Tyr 375 Asp Thr Pro Tyr Glu Pro Glu Gly Gln Ser Val Asp Ser Asp Ser Glu 390 395 Ser Thr Val Ser Pro Arg Leu Arg Glu Ser Lys Leu Pro Gln Asp Asp 410

```
Asp Arg Pro Ala Asp Glu Tyr Asp Gln Pro Trp Glu Trp Asn Arg Val
            420
                              425
Thr Ser Pro Ala Leu Ala Ala Gln Phe Asn Gly Asn Glu Lys Arg Gln
                            440
Ser Ser Pro Ser Pro Ser Arg Asp Arg Arg Arg Gln Leu Arg Ala Pro
                        455
Gly Gly Phe Lys Pro Ile Lys His Gly Ser Pro Glu Phe Cys Gly
                    470
                                       475
Ile Leu Gly Glu Arg Val Asp Pro Ala Val Pro Leu Glu Lys Gln Ile
                                   490
Trp Tyr His Gly Ala Ile Ser Arg Gly Asp Ala Glu Asn Leu Leu Arg
            500
                                505
Leu Cys Lys Glu Cys Ser Tyr Leu Val Arg Asn Ser Gln Thr Ser Lys
                           520
His Asp Tyr Pro Leu Ser Leu Arg Ser Asn Gln Gly Phe Met His Met
                        535
Lys Leu Ala Lys Thr Lys Glu Lys Tyr Val Leu Gly Gln Asn Ser Pro
                    550
Pro Phe Asp Ser Val Pro Glu Val Ile His Tyr Tyr Thr Thr Arg Lys
                565
                                    570
Leu Pro Ile Lys Gly Ala Glu His Leu Ser Leu Leu Tyr Pro Val Ala
                               585
Val Arg Thr Leu
        595
      <210> 82
      <211> 207
      <212> PRT
      <213> Homo Sapiens
     <400> 82
Met Ser Pro Leu Leu Arg Arg Leu Leu Leu Ala Ala Leu Leu Gln Leu
                                    10
Ala Pro Ala Gln Ala Pro Val Ser Gln Pro Asp Ala Pro Gly His Gln
                                25
Arg Lys Val Val Ser Trp Ile Asp Val Tyr Thr Arg Ala Thr Cys Gln
                           40
Pro Arg Glu Val Val Val Pro Leu Thr Val Glu Leu Met Gly Thr Val
                       55
Ala Lys Gln Leu Val Pro Ser Cys Val Thr Val Gln Arg Cys Gly Gly
                   70
                                       75
Cys Cys Pro Asp Asp Gly Leu Glu Cys Val Pro Thr Gly Gln His Gln
                                   90
Val Arg Met Gln Ile Leu Met Ile Arg Tyr Pro Ser Ser Gln Leu Gly
                               105
Glu Met Ser Leu Glu Glu His Ser Gln Cys Glu Cys Arg Pro Lys Lys
                           120
Lys Asp Ser Ala Val Lys Pro Asp Arg Ala Ala Thr Pro His His Arg
                       135
Pro Gln Pro Arg Ser Val Pro Gly Trp Asp Ser Ala Pro Gly Ala Pro
                   150
                                       155
Ser Pro Ala Asp Ile Thr His Pro Thr Pro Ala Pro Gly Pro Ser Ala
                                  170
His Ala Ala Pro Ser Thr Thr Ser Ala Leu Thr Pro Gly Pro Ala Ala
           180
                               185
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Ala Ala Ala Asp Ala Ala Ala Ser Ser Val Ala Lys Gly Gly Ala <210> 83 <211> 429 <212> PRT <213> Homo Sapiens <400> 83 Glu Cys Asp Val Met .Thr Tyr Val Arg Glu Thr Cys Gly Cys Cys Asp 10 Cys Glu Lys Arg Cys Gly Ala Leu Asp Val Val Phe Val Ile Asp Ser 25 Ser Glu Ser Ile Gly Tyr Thr Asn Phe Thr Leu Glu Lys Asn Phe Val 40 Ile Asn Val Val Asn Arg Leu Gly Ala Ile Ala Lys Asp Pro Lys Ser Glu Thr Gly Thr Arg Val Gly Val Val Gln Tyr Ser His Glu Gly Thr 75 Phe Glu Ala Ile Gln Leu Asp Asp Glu His Ile Asp Ser Leu Ser Ser 90 Phe Lys Glu Ala Val Lys Asn Leu Glu Trp Ile Ala Gly Gly Thr Trp 105 Thr Pro Ser Ala Leu Lys Phe Ala Tyr Asp Arg Leu Ile Lys Glu Ser 120 Arg Arg Gln Lys Thr Arg Val Phe Ala Val Val Ile Thr Asp Gly Arg 135 His Asp Pro Arg Asp Asp Leu Asn Leu Arg Ala Leu Cys Asp Arg 150 155 Asp Val Thr Val Thr Ala Ile Gly Ile Gly Asp Met Phe His Glu Lys 170 His Glu Ser Glu Asn Leu Tyr Ser Ile Ala Cys Asp Lys Pro Gln Gln 185 Val Arg Asn Met Thr Leu Phe Ser Asp Leu Val Ala Glu Lys Phe Ile 200 Asp Asp Met Glu Asp Val Leu Cys Pro Asp Pro Gln Ile Val Cys Pro 215 220 Asp Leu Pro Cys Gln Thr Glu Leu Ser Val Ala Gln Cys Thr Gln Arg 230 235 Pro Val Asp Ile Val Phe Leu Leu Asp Gly Ser Glu Arg Leu Gly Glu 245 250 Gln Asn Phe His Lys Ala Arg Arg Phe Val Glu Gln Val Ala Arg Arg 265 Leu Thr Leu Ala Arg Arg Asp Asp Pro Leu Asn Ala Arg Val Ala 280 Leu Leu Gln Phe Gly Gly Pro Gly Glu Gln Gln Val Ala Phe Pro Leu 295 Ser His Asn Leu Thr Ala Ile His Glu Ala Leu Glu Thr Thr Gln Tyr 310 315 Leu Asn Ser Phe Ser His Val Gly Ala Gly Val Val His Ala Ile Asn 325 330 Ala Ile Val Arg Ser Pro Arg Gly Gly Ala Arg Arg His Ala Glu Leu 345 Ser Phe Val Phe Leu Thr Asp Gly Val Thr Gly Asn Asp Ser Leu His 355 360

Glu Ser Ala His Ser Met Arg Asn Glu Asn Val Val Pro Thr Val Leu 375 Ala Leu Gly Ser Asp Val Asp Met Asp Val Leu Thr Thr Leu Ser Leu 390 395 Gly Asp Arg Ala Ala Val Phe His Glu Lys Asp Tyr Asp Ser Leu Ala 410 Gln Pro Gly Phe Phe Asp Arg Phe Ile Arg Trp Ile Cys <210> 84 <211> 113 <212> PRT <213> Homo Sapiens <400> 84 Met Ser Ala Ser Val Val Ser Val Ile Ser Arg Phe Leu Glu Glu Tyr 10 Leu Ser Ser Thr Pro Gln Arg Leu Lys Leu Leu Asp Ala Tyr Leu Leu Tyr Ile Leu Leu Thr Gly Ala Leu Gln Phe Gly Tyr Cys Leu Leu Val 40 Gly Thr Phe Pro Phe Asn Ser Phe Leu Ser Gly Phe Ile Ser Cys Val Gly Ser Phe Ile Leu Ala Val Cys Leu Arg Ile Gln Ile Asn Pro Gln 75 Asn Lys Ala Asp Phe Gln Gly Ile Ser Pro Glu Arg Ala Phe Ala Asp 90 Phe Leu Phe Ala Ser Thr Ile Leu His Leu Val Val Met Asn Phe Val Gly <210> 85 <211> 258 <212> PRT <213> Homo Sapiens <400> 85 Met Ile Asn Ile Glu Ser Met Asp Thr Asp Lys Asp Asp Pro His Gly 10 Arg Leu Glu Tyr Thr Glu His Gln Gly Arg Ile Lys Asn Ala Arg Glu 25 Ala His Ser Gln Ile Glu Lys Arg Arg Arg Asp Lys Met Asn Ser Phe Ile Asp Glu Leu Ala Ser Leu Val Pro Thr Cys Asn Ala Met Ser Arg Lys Leu Asp Lys Leu Thr Val Leu Arg Met Ala Val Gln His Met Lys 70 75 Thr Leu Arg Gly Ala Thr Asn Pro Tyr Thr Glu Ala Asn Tyr Lys Pro 90 Thr Phe Leu Ser Asp Asp Glu Leu Lys His Leu Ile Leu Arg Ala Ala 105 Asp Gly Phe Leu Phe Val Val Gly Cys Asp Arg Gly Lys Ile Leu Phe

115 120 125 Val Ser Glu Ser Val Phe Lys Ile Leu Asn Tyr Ser Gln Asn Asp Leu

130 135 Ile Gly Gln Ser Leu Phe Asp Tyr Leu His Pro Lys Asp Ile Ala Lys 150 155 Val Lys Glu Gln Leu Ser Ser Ser Asp Thr Ala Pro Arg Glu Arg Leu 165 170 Ile Asp Ala Lys Thr Gly Leu Pro Val Lys Thr Asp Ile Thr Pro Gly 185 Pro Ser Arg Leu Cys Ser Gly Ala Arg Arg Ser Phe Phe Cys Arg Met 200 Lys Cys Asn Arg Pro Ser Val Asn Val Glu Asp Lys Asn Phe Pro Ser 215 220 Thr Cys Ser Lys Lys Lys Ala Asp Arg Lys Ala Phe Cys Thr Ile His 230 235 Ser Thr Gly Tyr Phe Gly Ile Phe Thr Thr Arg Thr Ser Arg His Ile 245 Val Leu

<210> 86

<211> 569

<212> PRT

<213> Homo Sapiens

<400> 86

Met Ser Thr Met Val Tyr Ile Lys Glu Asp Lys Leu Glu Lys Leu Thr 10 Gln Asp Glu Ile Ile Ser Lys Thr Lys Gln Val Ile Gln Gly Leu Glu Ala Leu Lys Asn Glu His Asn Ser Ile Leu Gln Ser Leu Leu Glu Thr 40 Leu Lys Cys Leu Lys Lys Asp Asp Glu Ser Asn Leu Val Glu Glu Lys 55 Ser Asn Met Ile Arg Lys Ser Leu Glu Met Leu Glu Leu Gly Leu Ser 70 Glu Ala Gln Val Met Met Ala Leu Ser Asn His Leu Asn Ala Val Glu 85 90 Ser Glu Lys Gln Lys Leu Arg Ala Gln Val Arg Arg Leu Cys Gln Glu 105 Asn Gln Trp Leu Arg Asp Glu Leu Ala Asn Thr Gln Gln Lys Leu Gln 120 Lys Ser Glu Gln Ser Val Ala Gln Leu Glu Glu Glu Lys Lys His Leu 135 Glu Phe Met Asn Gln Leu Lys Lys Tyr Asp Asp Asp Ile Ser Pro Ser 155 Glu Asp Lys Asp Thr Asp Ser Thr Lys Glu Pro Leu Asp Asp Leu Phe 170 Pro Asn Asp Glu Asp Asp Pro Gly Gln Gly Ile Gln Gln His Ser Ser Ala Ala Ala Ala Gln Gln Gly Gly Tyr Glu Ile Pro Ala Arg 200 Leu Arg Thr Leu His Asn Leu Val Ile Gln Tyr Ala Ser Gln Gly Arg 215 Tyr Glu Val Ala Val Pro Leu Cys Lys Gln Ala Leu Glu Asp Leu Glu 235 Lys Thr Ser Gly His Asp His Pro Asp Val Ala Thr Met Leu Asn Ile

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245
                                    250
Leu Ala Leu Val Tyr Arg Asp Gln Asn Lys Tyr Lys Asp Ala Ala Asn
                              265
Leu Leu Asn Asp Ala Leu Ala Ile Arg Glu Lys Thr Leu Gly Lys Asp
                           280
His Pro Ala Val Ala Ala Thr Leu Asn Asn Leu Ala Val Leu Tyr Gly
                       295
Lys Arg Gly Lys Tyr Lys Glu Ala Glu Pro Leu Cys Lys Arg Ala Leu
                   310
                                       315
Glu Ile Arg Glu Lys Val Leu Gly Lys Asp His Pro Asp Val Ala Lys
                                   330
Gln Leu Asn Asn Leu Ala Leu Leu Cys Gln Asn Gln Gly Lys Tyr Glu
            340
                               345
Glu Val Glu Tyr Tyr Tyr Gln Arg Ala Leu Glu Ile Tyr Gln Thr Lys
                           360
Leu Gly Pro Asp Asp Pro Asn Val Ala Lys Thr Lys Asn Asn Leu Ala
                       375
Ser Cys Tyr Leu Lys Gln Gly Lys Phe Lys Gln Ala Glu Thr Leu Tyr
                   390
Lys Glu Ile Leu Thr Arg Ala His Glu Arg Glu Phe Gly Ser Val Asp
                                   410
Asp Glu Asn Lys Pro Ile Trp Met His Ala Glu Glu Arg Glu Glu Cys
                               425
Lys Gly Lys Gln Lys Asp Gly Thr Ser Phe Gly Glu Tyr Gly Gly Trp
                           440
Tyr Lys Ala Cys Lys Val Asp Ser Pro Thr Val Thr Thr Leu Lys
                       455
Asn Leu Gly Ala Leu Tyr Arg Arg Gln Gly Lys Phe Glu Ala Ala Glu
                   470
                                       475
Thr Leu Glu Glu Ala Ala Met Arg Ser Arg Lys Gln Gly Leu Asp Asn
                                   490
Val His Lys Gln Arg Val Ala Glu Val Leu Asn Asp Pro Glu Asn Met
                               505
Glu Lys Arg Arg Ser Arg Glu Ser Leu Asn Val Asp Val Val Lys Tyr
                           520
Glu Ser Gly Pro Asp Gly Gly Glu Glu Val Ser Met Ser Val Glu Trp
                       535
                                           540
Asn Gly Gly Val Ser Gly Arg Ala Ser Phe Cys Gly Lys Arg Gln Gln
                   550
                                      555
Gln Gln Trp Pro Gly Arg Arg His Arg
               565
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     <211> 736
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<212> PRT

<213> Homo Sapiens

<400> 87

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Leu 65	Gln	Leu	Val	His	Val 70	Thr	Gln	Glu	Asp	Lys 75	Arg	Lys	Thr	Thr	Gly 80
Glu	Glu	Asn	Gly	Val 85	Glu	Ala	Glu	Glu	Trp 90	Gly	Lys	Phe	Leu	His 95	Thr
			100		Thr			105					110	Ile	
Asn	Glu	Thr 115	Glu	Arg	Ile	Ser	Gly 120	Asn	Asn	Lys	Gly	Val 125	Ser	Pro	Glu
Pro	Ile 130	His	Leu	Lys	Ile	Phe 135	Ser	Pro	Asn	Val	Val 140	Asn	Leu	Thr	Leu
145					Met 150					155					160
				165	Ile				170					175	
			180		Leu			185					190		
		195			Lys		200					205			
	210				Ile	215					220				
225					Leu 230					235					240
				245	Asn				250					255	_
			260		Ile			265					270		
		275			Asn		280					285		_	
	290				Met	295					300				
305					Val 310					315					320
				325	Val				330					335	
			340		Thr			345					350		
		355			Ser		360					365			
	370				Phe	375					380				
385					Ile 390					395					400
				405	Leu				410					415	
			420		Lys			425					430	_	
		435			Glu		440					445			
	450				Leu	455					460				
465					Cys 470					475					480
Glu	Met	Val	His	Asn 485	Leu	Val	Ala	Ile	Glu 490	Leu	Ala	Tyr	Ile	Asn 495	Thr

```
Lys His Pro Asp Phe Ala Asp Ala Cys Gly Leu Met Asn Asn Ile
           500
Glu Glu Gln Arg Arg Asn Arg Leu Ala Arg Glu Leu Pro Ser Ala Val
                          520
                                             525
Ser Arg Asp Lys Ser Ser Lys Val Pro Ser Ala Leu Ala Pro Ala Ser
                       535
Gln Glu Pro Ser Pro Ala Ala Ser Ala Glu Ala Asp Gly Lys Leu Ile
                   550
                                      555
Gln Asp Ser Arg Arg Glu Thr Lys Asn Val Ala Ser Gly Gly Gly Gly
                                   570
Val Gly Asp Gly Val Gln Glu Pro Thr Thr Gly Asn Trp Arg Gly Met
                               585
Leu Lys Thr Ser Lys Ala Glu Glu Leu Leu Ala Glu Glu Lys Ser Lys
                           600
Pro Ile Pro Ile Met Pro Ala Ser Pro Gln Lys Gly His Ala Val Asn
                       615
Leu Leu Asp Val Pro Val Pro Val Ala Arg Lys Leu Ser Ala Arg Glu
                   630
                                       635
Gln Arg Asp Cys Glu Val Ile Glu Arg Leu Ile Lys Ser Tyr Phe Leu
               645
                                   650
Ile Val Arg Lys Asn Ile Gln Asp Ser Val Pro Lys Ala Val Met His
           660
                              665
                                                  670
Phe Leu Val Asn His Val Lys Asp Thr Leu Gln Ser Glu Leu Val Gly
                          680
Gln Leu Tyr Lys Ser Ser Leu Leu Asp Asp Leu Leu Thr Glu Ser Glu
                       695
Asp Met Ala Gln Arg Arg Lys Glu Ala Ala Asp Met Leu Lys Ala Leu
                  710
                                      715
Gln Gly Ala Ser Gln Ile Ile Ala Glu Ile Arg Glu Thr His Leu Trp
               725
                                   730
      <210> 88
      <211> 37
      <212> PRT
      <213> Homo Sapiens
      <400> 88
Met Gly Asp His Ala Trp Ser Phe Leu Lys Asp Phe Leu Ala Gly Gly
                                   10
Val Ala Ala Ala Val Ser Lys Thr Ala Val Ala Pro Ile Glu Arg Val
           20
                               25
Lys Leu Leu Leu Gln
       35
      <210> 89
      <211> 1381
      <212> DNA
      <213> Homo Sapiens
      <400> 89
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                                                                     60
gcgttcgtgt ccgagttctc tgcaggtcnc tantttcccg gtagttcanc tgcncatgaa
                                                                     120
tanaacagca atgagagccn ctcncaaaga ctttgaaaat tcactgaatc nagtgaaact
                                                                     180
ctngaaaaag gatccangaa acgaaatgaa nctnaaactc tncgcgctat atnancangc
                                                                     240
cnctgaanga cttgtntcat gcccnaacca ngtgtntttg acttgatcna caaggggcca
```

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atgggacaca tggaatgccc ttggcancct gcccnaagaa ctgccaggca naactatgtg
                                                                      360
gatttggtgt ccantttgan tecntecttg gaateetena atenngtgga neetggaaca
                                                                      420
nacaggaaat ccactgggtt tgaaactctg gtggtgacct ccgaagatgg catcacaaag
                                                                      480
atcatgttca accggcccaa aaagaaaaat gccataaaca ctgagatgta tcatgaaatt
                                                                      540
atgcgtgcac ttaaagctgc cagcaaggat gactcaatca tcactgtttt aacaggaaat
                                                                      600
ggtgactatt acagtagtgg gaatgatctg actaacttca ctgatattcc ccctggtgga
                                                                      660
gtagaggaga aagctaaaaa taatgccgtt ttactgaggg aatttgtggg ctgttttata
                                                                      720
gattttccta agcctctgat tgcagtggtc aatggtccag ctgtgggcat ctccgtcacc
                                                                      780
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PCT/US98/14679 WO 99/04265

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Pro	HIS	Pne	100	PIO	Asp	Ата	Met	105	GIY	GIII	PLO	GIA	110	Leu	GIY
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Lys Asp Gly Lys Lys Cys Leu Phe Leu Val Lys Cys Phe Asp Lys Thr
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His Ser Thr Ile His Leu Leu Lys Leu Ser Pro Pro Pro Lys Glu Ala
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PCT/US98/14679 WO 99/04265

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960

983

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 Fyr
 Fy

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1920

1980

2040

2100

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345

340

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<212> PRT

<213> Homo Sapiens

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Pro Ser Ser Ala Lys Gly Pro Val Phe Ser Val Pro Val Gly Glu Ile 200 Lys Pro Gln Gly Val Tyr Asp Ile Pro Pro Thr Lys Gly Val Tyr Ala 215 220 Ile Pro Pro Ser Ala Cys Arg Asp Glu Ala Gly Leu Arg Glu Lys Asp 230 235 Tyr Asp Phe Pro Pro Pro Met Arg Gln Ala Gly Arg Pro Asp Leu Arg 250 Pro Glu Gly Val Tyr Asp Ile Pro Pro Thr Cys Thr Lys Pro Ala Gly 265 Lys Asp Leu His Val Lys Tyr Asn Cys Asp Ile Pro Gly Ala Ala Glu 280 Pro Val Ala Arg Arg His Gln Ser Leu Ser Pro Asn His Pro Pro 295 300 Gln Leu Gly Gln Ser Val Gly Ser Gln Asn Asp Ala Tyr Asp Val Pro 310 315 Arg Gly Val Gln Phe Leu Glu Pro Pro Ala Glu Thr Ser Glu Lys Ala 325 330 Asn Pro Gln Glu Arg Asp Gly Val Tyr Asp Val Pro Leu His Asn Pro 345 Pro Asp Ala Lys Gly Ser Arg Asp Leu Val Asp Gly Ile Asn Arg Leu 360 Ser Phe Ser Ser Thr Gly Ser Thr Arg Ser Asn Met Ser Thr Ser Ser 375 Thr Ser Ser Lys Glu Ser Ser Leu Ser Ala Ser Pro Ala Gln Asp Lys 390 395 Arg Leu Phe Leu Asp Pro Asp Thr Ala Ile Glu Arg Leu Gln Arg Leu 410 Gln Gln Ala Leu Glu Met Gly Val Ser Ser Leu Met Ala Leu Val Thr 425 Thr Asp Trp Arg Cys Tyr Gly Tyr Met Glu Arg His Ile Asn Glu Ile 435 440 Arg Thr Ala Val Asp Lys Val Glu Leu Phe Leu Lys Glu Tyr Leu His 455 460 Phe Val Lys Gly Ala Val Ala Asn Ala Ala Cys Leu Pro Glu Leu Ile 470 475 Leu His Asn Lys Met Lys Arg Glu Leu Gln Arg Val Glu Asp Ser His 485 490 Gln Ile Leu Ser Gln Thr Ser His Asp Leu Asn Glu Cys Ser Trp Ser 505 Leu Asn Ile Leu Ala Ile Asn Lys Pro Gln Asn Lys Cys Asp Asp Leu 520 525 Asp Arg Phe Val Met Val Ala Lys Thr Val Pro Asp Asp Ala Lys Gln 535 Leu Thr Thr Thr Ile Asn Thr Asn Ala Glu Ala Leu Phe Arg Pro Gly 550 555 Pro Gly Ser Leu His Leu Lys Asn Gly Pro Glu Ser Ile Met Asn Ser 570 Thr Glu Tyr Pro His Gly Gly Ser Gln Gly Gln Leu Leu His Pro Gly Asp His Lys Ala Gln Ala His Asn Lys Ala Leu Pro Pro Gly Leu Ser 600 Lys Glu Gln Ala Pro Asp Cys Ser Ser Ser Asp Gly Ser Glu Arg Ser 615 Trp Met Asp Asp Tyr Asp Tyr Val His Leu Gln Gly Lys Glu Glu Phe

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Arg Gln Leu Leu Cys Phe Tyr Tyr Asp Gln Cys Glu Thr His Phe Ile
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<211> 3429

<212> DNA

<213> Homo Sapiens

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<211> 906

<212> PRT

<213> Homo Sapiens

<400> 114

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 Asp
 Pro
 Lys

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 Glu
 Ile
 Arg
 Thr
 Leu
 Ala
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 Pro
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	Ala 210					215					220				
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	Glu		420					425					430		
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465	Asn				470					475					480
	Glu -			485					490					495	
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Ile Arg Lys Ala Val Leu Met Ile Arg Thr Pro Glu Glu Leu Asp Asp
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Gln Thr Glu Asp Asp Gln Leu Ile Ala Gly Gln Ser Ala Arg Ala Ile
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Met Ala Gln Leu Pro Gln Glu Gln Lys Ala Lys Ile Ala Glu Gln Val
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Trp Asp Asp Ser Gly Asn Asp Ile Ile Val Leu Ala Lys Gln Met Cys
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Met Ile Met Met Glu Met Thr Asp Phe Thr Arg Gly Lys Gly Pro Leu
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Lys Asn Thr Ser Asp Val Ile Ser Ala Ala Lys Lys Ile Ala Glu Ala
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Gly Ser Arg Met Asp Lys Leu Gly Arg Thr Ile Ala Asp His Cys Pro
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Asp Ser Ala Cys Lys Gln Asp Leu Leu Ala Tyr Leu Gln Arg Ile Ala
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                                          780
Leu Tyr Cys His Gln Leu Asn Ile Cys Ser Lys Val Lys Ala Glu Val
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Ser Leu Ile Gln Ala Ala Lys Asn Leu Met Asn Ala Val Val Gln Thr
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                           825
Val Lys Ala Ser Tyr Val Ala Ser Thr Lys Tyr Gln Lys Ser Gln Gly
                           840
Met Ala Ser Leu Asn Leu Pro Ala Val Ser Trp Lys Met Lys Ala Pro
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Glu Lys Lys Pro Leu Val Lys Arg Glu Lys Gln Asp Glu Thr Gln Thr
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Lys Ile Lys Arg Ala Ser Gln Lys Lys His Val Asn Pro Val Gln Ala
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-83-

<400> 115

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                                                                      120
cctgataaga atccccaaat gcaggagaca aactttaaag aaataagttt tgcatatgaa
                                                                       180
gtactatcaa atcctgagaa gcgtgagtta tatgacagat acggagagca aggtcttcgg
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gaaggcagcg gcggaggtgg gtggcatgga ttgatatttt ctctcaccgt tttttgtggg
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<210> 116

<211> 415

<212> PRT

<213> Homo Sapiens

<400> 116

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145
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Cys Ser Ala Cys Arg Gly Arg Gly Val Arg Ile Met Ile Arg Gln Leu
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Ala Pro Gly Met Val Gln Gln Met Gln Ser Val Cys Ser Asp Cys Asn
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Gly Glu Gly Glu Val Ile Asn Glu Lys Asp Arg Cys Lys Lys Cys Glu
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                            200
Gly Lys Lys Val Ile Lys Glu Val Lys Ile Leu Glu Val His Val Asp
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                                            220
Lys Gly Met Lys His Gly Gln Arg Ile Thr Phe Thr Gly Glu Ala Asp
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                                        235
Gln Ala Pro Glu Trp Asn Pro Glu Thr Leu Phe Phe Leu Leu Pro Gly
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Glu Lys Asn Met Glu Val Phe Gln Arg Asp Gly Asn Asp Leu His Met
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Thr Tyr Lys Ile Gly Leu Val Glu Ala Leu Cys Gly Phe Gln Phe Thr
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Leu Ser His Leu Asp Gly Arg Gln Ile Val Val Lys Tyr Pro Pro Gly
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Lys Val Ile Glu Pro Gly Cys Val Arg Val Val Arg Gly Glu Gly Met
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Pro Gln Tyr Arg Asn Pro Phe Glu Lys Gly Gly Leu Tyr Ile Lys Phe
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                                    330
Asp Val Gln Phe Pro Glu Asn Asn Trp Ile Asn Pro Asp Lys Leu Ser
                                345
                                                    350
Glu Leu Glu Asp Leu Leu Pro Ser Arg Pro Glu Val Pro Asn Ile Ile
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Gly Glu Thr Glu Glu Val Glu Leu Gln Glu Phe Asp Ser Thr Arg Gly
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Ser Gly Gly Gln Arg Arg Glu Ala Tyr Asn Asp Ser Ser Asp Glu
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<210> 117

<211> 1821

<212> DNA

<213> Homo Sapiens

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<210> 118

<211> 548

<212> PRT

<213> Homo Sapiens

<400> 118

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Val Leu Ile Lys Thr Ala Glu Glu Leu Met Asn Phe Ser Lys Gly Glu
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Asn Val Val Val Thr Gly Gly Lys Val Ala Asp Met Ala Leu His Tyr
                        295
Ala Asn Lys Tyr Asn Ile Met Leu Val Arg Leu Asn Ser Lys Trp Asp
305
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Leu Arg Arg Leu Cys Lys Thr Val Gly Ala Thr Ala Leu Pro Arg Leu
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Thr Pro Pro Val Leu Glu Glu Met Gly His Cys Asp Ser Val Tyr Leu
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Ser Glu Val Gly Asp Thr Gln Val Val Phe Lys His Glu Lys Glu
                            360
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Asp Gly Ala Ile Ser Thr Ile Val Leu Arg Gly Ser Thr Asp Asn Leu
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Met Asp Asp Ile Glu Arg Val Val Asp Asp Gly Val Asn Thr Phe Lys
                    390
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Val Leu Thr Arg Asp Lys Arg Leu Val Pro Gly Gly Gly Ala Thr Glu
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Ile Glu Leu Ala Lys Gln Ile Thr Ser Tyr Gly Glu Thr Cys Pro Gly
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Leu Glu Gln Tyr Ala Ile Lys Lys Phe Ala Glu Ala Phe Glu Ala Ile
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Ser Lys Leu Tyr Ala Val His Gln Glu Gly Asn Lys Asn Val Gly Leu
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                                         475
Asp Ile Glu Ala Glu Val Pro Ala Val Lys Asp Met Leu Glu Ala Gly
                485
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Ile Leu Asp Thr Tyr Leu Gly Lys Tyr Trp Ala Ile Lys Leu Ala Thr
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Asn Ala Ala Val Thr Val Leu Arg Val Asp Gln Ile Ile Met Ala Lys
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                                                                       480
aaatacagag atacaagcag aagaaggagt tggagcatag gttgtctgca atgaaatctg
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ctccagtgaa	accettcatt	ctcactcgga	acatggctca	agccaaagta	tttggagctg	780
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gagcattacc	ggatcaggga	atagccaagg	cagcaccaga	ggaattcaga	aaagcagctc	900
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gatgatatga	accagcagtc	ttgttttggc	atcatcctca	tcatgttgta	ttccagcttc	1260
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<210> 120

<211> 339

<212> PRT

<213> Homo Sapiens

<400> 120

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<210> 121 <211> 2965 <212> DNA <213> Homo Sapiens

<400> 121

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<211> 862

<212> PRT

<213> Homo Sapiens

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	290					295					300	)			
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Lys	Ala	Asp	Val 340	Glu	Glu	Glu	Ile	Lys	Ile		Val	Val	. Cys	Ala	Leu
Thr	Gln	Glu 355	Glu		Ser	Ala	Gln 360	Leu		Asn	Glu		Glu	His	Leu
Asp	Ser 370	Thr		Gly	Ser				Leu	Asp				Leu	Leu
Pro			Asp	Pro	Phe	375 Ser	Tare	Sar	7 00	7 an	380	Mat	Dh.a		
385		1			390	DCI	цуз	Ser	нар	395	Asp	Met	Pne	гуs	Asp 400
Gly	Leu	Arg	Arg	Ala	Gln	Ser	Thr	Asp	Ser		Gly	Thr	Ser	Glv	Ser
				405					410					415	
			420		Leu			425					430		
		435			Asp		440					445			
Ser	Glu 450	Asn	Phe	Asp	Thr	Ala 455	Ser	Leu	Gly	Ser	Leu 460	Gln	Met	Pro	Ser
Gly	Phe	Met	Leu	Thr	Lys	Asp	Gln	Glu	Arg	Ala	Ile	Lys	Ala	Met	Thr
465					470					475					480
				485	Thr				490					495	
			500		Val			505					510		
		515			Leu		520					525			_
	530				Asp	535					540				
Gly 545	Ile	Gln	Ile	Gln	Glu 550	Ala	Glu	Thr	Arg	Asp 555	Gln	Val	Lys	Lys	Leu 560
Gln	Leu	Met	Leu	Arg 565	Gln	Ala	Asn	Asp	Gln 570	Leu	Glu	Lys	Thr	Met 575	Lys
Asp	Lys	Gln	Glu 580	Leu	Glu	Asp	Phe	Ile 585		Gln	Ser	Ser	Glu 590	Asp	Ser
Ser	His	Gln 595	Ile	Ser	Ala	Leu	Val 600		Arg	Ala	Gln	Ala 605	Ser	Glu	Ile
Leu	Leu 610	Glu	Glu	Leu	Gln	Gln 615	Gly		Ser		Ala 620	Lys	Arg	Asp	Val
Gln	Glu	Gln	Met	Ala	Val	Leu	Met	Gln	Ser				Val	Ser	Glu
625					630					635					640
				645	Gln				650					655	His
Ser	Leu	His	Val 660	Ser	Leu	Gln	Gln	Ala 665	Glu	Asp	Phe	Ile	Leu 670	Pro	Asp
Thr	Thr	Glu 675	Ala	Leu	Arg	Glu	Leu 680	Val	Leu	Lys .	Tyr	Arg 685	Glu	Asp	Ile
Ile	Asn 690	Val	Arg	Thr	Ala	Ala 695		His	Val	Glu	Glu 700		Leu	Lys	Ala
Glu 705	Ile	Leu	Phe	Leu	Lys 710		Gln	Ile	Gln	Ala 715	Glu	Gln	Cys	Leu	
Glu	Asn	Leu	Glu	Glu 725	Thr	Leu	Gln	Leu	Glu 730		Glu	Asn	Сув	Lys 735	720 Glu

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Glu Ile Ala Ser Ile Ser Ser Leu Lys Ala Glu Leu Glu Arg Ile Lys
            740
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Val Glu Lys Gly Gln Leu Glu Ser Thr Leu Arg Glu Lys Ser Gln Gln
                            760
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Leu Glu Ser Leu Gln Glu Ile Lys Ile Ser Leu Glu Glu Gln Leu Lys
                        775
Lys Glu Thr Ala Ala Lys Ala Thr Val Glu Gln Leu Met Phe Glu Glu
                   790
                                        795
Lys Asn Lys Ala Gln Arg Leu Gln Thr Glu Leu Asp Val Ser Glu Gln
                                810
Val Gln Arg Asp Phe Val Lys Leu Ser Gln Thr Leu Gln Val Gln Leu
            820
                               825
                                                   830
Glu Arg Ile Arg Gln Ala Asp Ser Leu Glu Arg Ile Arg Ala Ile Leu
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                                               845
Asn Asp Thr Lys Leu Thr Asp Ile Asn Gln Leu Pro Glu Thr
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ttqqtttqqc attaaaggac cttgctaagc agtactctga caqactagaa tqctqtqaaa
                                                                      180
atgaagtaga aaaggtaata gaagaaatac gttgcaaggc aattgagcgt ggaacaggaa
                                                                      240
atgacaatta tagaacaacg ggaattgcta caatcgaggt gtttttacca ccaagactaa
                                                                      300
aaaaagatag gaaaaacttg ttggagaccc gattgcacat cactggcaga gaactgaggt
                                                                      360
ccaaaatagc tgaaaccttt ggacttcaag aanattatat caaaattgtc ataaataaga
                                                                      420
agcaactacn actagggaaa accettgaag ancaaggegt ggetcacaat gtgaaagega
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tggtgcttga actaaaacaa tctgaagagg acgcgaggaa aaacttccag ttagaggaag
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agga
                                                                      544
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Leu Thr Gln Phe Leu Arg Glu Asp Arg Ile Gln Leu Trp Lys Pro Pro
                                25
Tyr Thr Asp Glu Asn Lys Lys Val Gly Leu Ala Leu Lys Asp Leu Ala
                            40
Lys Gln Tyr Ser Asp Arg Leu Glu Cys Cys Glu Asn Glu Val Glu Lys
                        55
Val Ile Glu Glu Ile Arg Cys Lys Ala Ile Glu Arg Gly Thr Gly Asn
                    70
                                        75
Asp Asn Tyr Arg Thr Thr Gly Ile Ala Thr Ile Glu Val Phe Leu Pro
Pro Arg Leu Lys Lys Asp Arg Lys Asn Leu Leu Glu Thr Arg Leu His
                                105
Ile Thr Gly Arg Glu Leu Arg Ser Lys Ile Ala Glu Thr Phe Gly Leu
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60

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115
                            120
                                               125
Gln Glu Tyr Ile Lys Ile Val Ile Asn Lys Lys Gln Leu Leu Gly Lys
                        135
                                           140
Thr Leu Glu Gln Gly Val Ala His Asn Val Lys Ala Met Val Leu Glu
145
                    150
                                       155
Leu Lys Gln Ser Glu Glu Asp Ala Arg Lys Asn Phe Gln Leu Glu Glu
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                                    170
Glu Glu
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                                                                     180
ggcaaggtga aggaggtgct ggactcggag acgctgtgca ggagggccgt caagatcctc
                                                                     240
aagaagaaga agttgcgaag gatccccaac ggggaggcca acgtgaagaa ggaaattcaa
                                                                     300
ctactgagga ggttacggca caaaaatgtc atccagctgg tggatgtgtt atacaacgaa
                                                                     360
gagaagcaga aaatgtatat ggtgatggag tactgcgtgt gtggcatgca ggaaatgctg
                                                                     420
gacagcgtgc cggagaagcg tttcccagtg tgccaggccc acgggtactt ctgtcagctg
                                                                     480
attgacggcc tggagtacct gcatagccag ggcattgtgc acaaggacat caagccgggg
                                                                     540
aacctgctgc tcaccaccgg tggcaccctc aaaatctccg acctgggcgt ggccgaggca
                                                                     600
ctgcacccgt tcgcggcgga cgacacctgc cggaccagcc agggctcccc ggctttccag
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ccgcccgaga ttgccaacgg cctggacacc ttctccggct tcaaggtgga catctggtcg
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getggggtea ceetetacaa catcaccaeg ggtetgtace cettegaagg ggacaacate
                                                                     780
tacaagttgt ttgagaacat cgggaagggg agctacgcca tcccqqqcqa ctqtqqccc
                                                                     840
cegetetetg acetgetgaa agggatgett gagtacgaac eggecaagag gttetecate
                                                                     900
cggcagatcc ggcagcacag ctggttccgg aagaaacatc ctccggctga agcaccagtg
                                                                     960
cccatcccac cgagcccaga caccaaggac cggtggcgca gcatgactgt ggtgccgtac
                                                                    1020
ttggaggacc tgcacggcgc ggacgaggac gaggacctct tcgacatcga ggatgacatc
                                                                    1080
atctacactc aggacttcac ggtgcccgga caggtcccag aagaggaggc cagtcacaat
                                                                    1140
ggacagegee ggggceteee caaggeegtg tgtatgaacg gcacagagge ggegeagetg
                                                                    1200
agcaccaaat ccagggcgga gggccgggcc cccaaccctg cccgcaaggc ctgctccgcc
                                                                    1260
agcagcaaga teegeegget gteggeetge aagcagcagt ga
                                                                    1302
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Leu Met Ser Val Gly Met Asp Thr Phe Ile His Arg Ile Asp Ser Thr
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Glu Val Ile Tyr Gln Pro Arg Arg Lys Arg Ala Lys Leu Ile Gly Lys
                           40
Tyr Leu Met Gly Asp Leu Leu Gly Glu Gly Ser Tyr Gly Lys Val Lys
                                           60
Glu Val Leu Asp Ser Glu Thr Leu Cys Arg Arg Ala Val Lys Ile Leu
                   70
                                       75
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Lys Lys Lys Leu Arg Arg Ile Pro Asn Gly Glu Ala Asn Val Lys
Lys Glu Ile Gln Leu Leu Arg Arg Leu Arg His Lys Asn Val Ile Gln
                               105
Leu Val Asp Val Leu Tyr Asn Glu Glu Lys Gln Lys Met Tyr Met Val
                          120
Met Glu Tyr Cys Val Cys Gly Met Gln Glu Met Leu Asp Ser Val Pro
                      135
Glu Lys Arg Phe Pro Val Cys Gln Ala His Gly Tyr Phe Cys Gln Leu
                   150
                                       155
Ile Asp Gly Leu Glu Tyr Leu His Ser Gln Gly Ile Val His Lys Asp
               165
                                  170
Ile Lys Pro Gly Asn Leu Leu Leu Thr Thr Gly Gly Thr Leu Lys Ile
                               185
Ser Asp Leu Gly Val Ala Glu Ala Leu His Pro Phe Ala Ala Asp Asp
                          200
                                              205
Thr Cys Arg Thr Ser Gln Gly Ser Pro Ala Phe Gln Pro Pro Glu Ile
                      215
Ala Asn Gly Leu Asp Thr Phe Ser Gly Phe Lys Val Asp Ile Trp Ser
                   230
                                       235
Ala Gly Val Thr Leu Tyr Asn Ile Thr Thr Gly Leu Tyr Pro Phe Glu
                                   250
Gly Asp Asn Ile Tyr Lys Leu Phe Glu Asn Ile Gly Lys Gly Ser Tyr
                               265
Ala Ile Pro Gly Asp Cys Gly Pro Pro Leu Ser Asp Leu Leu Lys Gly
                           280
Met Leu Glu Tyr Glu Pro Ala Lys Arg Phe Ser Ile Arg Gln Ile Arg
                       295
                                          300
Gln His Ser Trp Phe Arg Lys Lys His Pro Pro Ala Glu Ala Pro Val
                   310
                                      315
Pro Ile Pro Pro Ser Pro Asp Thr Lys Asp Arg Trp Arg Ser Met Thr
               325
                                  330
Val Val Pro Tyr Leu Glu Asp Leu His Gly Ala Asp Glu Asp
                              345
Leu Phe Asp Ile Glu Asp Asp Ile Ile Tyr Thr Gln Asp Phe Thr Val
                          360
Pro Gly Gln Val Pro Glu Glu Glu Ala Ser His Asn Gly Gln Arg Arg
                       375
Gly Leu Pro Lys Ala Val Cys Met Asn Gly Thr Glu Ala Ala Gln Leu
                  390
                                      395
Ser Thr Lys Ser Arg Ala Glu Gly Arg Ala Pro Asn Pro Ala Arg Lys
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Ala Cys Ser Ala Ser Ser Lys Ile Arg Arg Leu Ser Ala Cys Lys Gln
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Gln
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<210> 127

<211> 1488

<212> DNA

<213> Homo Sapiens

<400> 127

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gaacttgctc gactgagaga ctcaggactc tcacagaagg aggaagagga ggacactttt
                                                                   180
attgaagaac aacaactaga agaagagaag ctattggaaa gagagaggca aagattacat
                                                                   240
gaggagtggt tgctaagaga gcagaaggca caagaagaat tcagaataaa gaaggaaaag
                                                                   300
gaagaggcgg ctaaaaaacg gcaagaagaa caagagagaa agttaaagga acaatgggaa
                                                                   360
420
gaggaagctt tgcagaagat gctggatcag gctgaaaatg agttggaaaa tggtaccaca
                                                                   480
tggcaaaacc cagaaccacc cgtggatttc agagtaatgg agaaggatcg agctaattgt
                                                                   540
cccttctaca gtaaaacagg agcttgcaga tttggagata gatgttcacg taaacataat
                                                                   600
ttcccaacat ccagtcctac ccttcttatt aagagcatgt ttacgacgtt tggaatggag
                                                                   660
cagtgcagga gggatgacta tgaccctgac gcaagcctgg agtacagcga ggaagaaacc
                                                                   720
taccaacagt tcctagactt ctatgaggat gtgttgcccg agttcaagaa cgtggggaaa
                                                                   780
gtgattcagt tcaaggtcag ctgcaatttg gaacctcacc tgaggggcaa tgtatatgtt
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gcaggacgac agctgcagtg tgaattctgc cccgtgaccc ggtggaaaat ggcgatttgt
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                                                                  1020
agaaatccca acaatgaatt ctgggaagct aatagagaca tctacttgtc tccagatcgg
                                                                  1080
actggctcct cctttgggaa gaactccgaa aggagggaga ggatgggcca ccacgacgac
                                                                  1140
tactacagca ggctgcgggg aaggagaaac cctagtccag accactccta caaaagaaat
                                                                  1200
ggggaatccg agaggaaaag tagtcgtcac agggggaaga aatctcacaa acgcacatca
                                                                  1260
aagagtcggg agaggcacaa ttcacgaagc agaggaagaa atagggaccg cagcagggac
                                                                  1320
cgcagccggg gccggggcag ccggagccgg agccggagcc ggagccgcag gagccgcgc
                                                                  1380
agccggagcc aaagttcctc taggtcccga agtcgtggca ggaggaggtc gggtaataga
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<210> 128

<211> 482

<212> PRT

<213> Homo Sapiens

<400> 128

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195
                           200
                                                205
Phe Gly Met Glu Gln Cys Arg Arg Asp Asp Tyr Asp Pro Asp Ala Ser
                       215
                                           220
Leu Glu Tyr Ser Glu Glu Glu Thr Tyr Gln Gln Phe Leu Asp Phe Tyr
                    230
                                       235
Glu Asp Val Leu Pro Glu Phe Lys Asn Val Gly Lys Val Ile Gln Phe
                245
                                   250
Lys Val Ser Cys Asn Leu Glu Pro His Leu Arg Gly Asn Val Tyr Val
            260
                               265
Gln Tyr Gln Ser Glu Glu Glu Cys Gln Ala Ala Leu Ser Leu Phe Asn
                           280
                                               285
Gly Arg Trp Tyr Ala Gly Arg Gln Leu Gln Cys Glu Phe Cys Pro Val
                       295
Thr Arg Trp Lys Met Ala Ile Cys Gly Leu Phe Glu Ile Gln Gln Cys
                   310
                                       315
Pro Arg Gly Lys His Cys Asn Phe Leu His Val Phe Arg Asn Pro Asn
               325
                                  330
Asn Glu Phe Trp Glu Ala Asn Arg Asp Ile Tyr Leu Ser Pro Asp Arg
           340
                               345
Thr Gly Ser Ser Phe Gly Lys Asn Ser Glu Arg Arg Glu Arg Met Gly
                                               365
His His Asp Asp Tyr Tyr Ser Arg Leu Arg Gly Arg Arg Asn Pro Ser
                       375
Pro Asp His Ser Tyr Lys Arg Asn Gly Glu Ser Glu Arg Lys Ser Ser
                   390
                                       395
Arg His Arg Gly Lys Lys Ser His Lys Arg Thr Ser Lys Ser Arg Glu
               405
                                   410
Arg His Asn Ser Arg Ser Arg Gly Arg Asn Arg Asp Arg Ser Arg Asp
                               425
Arg Ser Arg Gly Arg Gly Ser Arg Ser Arg Ser Arg Ser Arg
                           440
Arg Ser Arg Arg Ser Arg Ser Gln Ser Ser Ser Arg Ser Arg
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Gly Arg Arg Ser Gly Asn Arg Asp Arg Thr Val Gln Ser Pro Lys
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Ser Lys
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<210> 129

<211> 1663

<212> DNA

<213> Homo Sapiens

## <400> 129

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                                                                      780
ccctccacta cagaacacac ttggtggacc ggccctatga ctgtaagtgt ggaaaagctt
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agtgcaaaga ttgtggcaag gctttcagcg ggaaaggcag cctcattcgt cactatcgga
                                                                      960
tccacactgg ggagaagcct tatcagtgta acgaatgtgg gaagagcttc agtcagcatg
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cgggcctcag ctcccaccag agactccaca ccggagagaa gccatataag tgtaaggagt
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gtgggaaagc cttcaaccac agctccaact tcaataaaca ccacagaatc cacaccgggg
                                                                     1140
aaaagcccta ctggtgtcat cactgtggaa agaccttctg tagcaagtcc aatctttcca
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ttgtcgttgt tttaaacttt agaatctgaa aaccagaaag aagtcttgtc attgcagcag
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catcgattcc ggtgatagag tttgtatcac tcaacatcag gggatgcctg aggagtgcga
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gctccacage aacatggcag gcaggaggtc ctcagaaggt gtcaggaggt tccacactcg
                                                                     1440
ccagttcact ggagcagagt cccttcgcca cacttagggt cccagtaagc catgccagca
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ttaccttttg cgtagttaaa cagacgtgta tccagtctag ttaaggaaga aacattaaga
                                                                     1560
ttgtttaatt tttaacatat attcaagaat tttaatttgt aaagaattga gccacattga
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<210> 130

<211> 412

<212> PRT

<213> Homo Sapiens

<400> 130

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245
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                                                         255
Ser Asn Leu Thr Leu His Tyr Arg Thr His Leu Val Asp Arg Pro Tyr
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Asp Cys Lys Cys Gly Lys Ala Phe Gly Gln Ser Ser Asp Leu Leu Lys
                            280
His Gln Arg Met His Thr Glu Glu Ala Pro Tyr Gln Cys Lys Asp Cys
                        295
                                            300
Gly Lys Ala Phe Ser Gly Lys Gly Ser Leu Ile Arg His Tyr Arg Ile
                    310
                                        315
His Thr Gly Glu Lys Pro Tyr Gln Cys Asn Glu Cys Gly Lys Ser Phe
                325
                                    330
Ser Gln His Ala Gly Leu Ser Ser His Gln Arg Leu His Thr Gly Glu
            340
                                345
                                                    350
Lys Pro Tyr Lys Cys Lys Glu Cys Gly Lys Ala Phe Asn His Ser Ser
                            360
Asn Phe Asn Lys His His Arg Ile His Thr Gly Glu Lys Pro Tyr Trp
                        375
                                            380
Cys His His Cys Gly Lys Thr Phe Cys Ser Lys Ser Asn Leu Ser Lys
                    390
                                        395
His Gln Arg Val His Thr Gly Glu Gly Glu Ala Pro
                                    410
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tagtagettg caggaagate tggeteatae cegaaatgat gecaategat tacaggatge
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cattgctaag gtagaggatg aataccgagc cttccaagaa gaagctaaga aacaaattga
                                                                       240
agatttgaat atgacgttag aaaaattaag atcagacctg gatgaaaaag aaacagaaag
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gagtgacatg aaagaaacca tctttgaact tgaagatgaa gtagaacaac atcgtgctgt
                                                                       360
gaaacttcat gacaacctca ttatttctga tctagagaat acagttaaaa aactccagga
                                                                       420
ccaaaagcac gacatggaaa gagaaataaa gacactccac agaagacttc gggaagaatc
                                                                       480
tgcggaatgg cggcagtttc aggctgatct ccagactgca gtagtcattg caaatgacat
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taaatctgaa gcccaagagg agattggtga tctaaagcgc cgggtacatg aggctcaaga
                                                                       600
aaaaaatgag aaactcacaa aagaattgga ggaaataagt ccgccaagcc agaagangac
                                                                       660
gangccggta ttccantaca tgnatgcccg tgagagagaa tttggcaggc cttaaggcag
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ggaa
                                                                       724
      <210> 132
      <211> 218
      <212> PRT
      <213> Homo Sapiens
      <400> 132
Glu Asn Glu Lys Gln Lys Val Ala Glu Leu Tyr Ser Ile His Asn Ser
                                    10
Gly Asp Lys Ser Asp Ile Gln Asp Leu Leu Glu Ser Val Arg Leu Asp
            20
                                25
Lys Glu Lys Ala Glu Thr Leu Ala Ser Ser Leu Gln Glu Asp Leu Ala
        35
                            40
                                                 45
His Thr Arg Asn Asp Ala Asn Arg Leu Gln Asp Ala Ile Ala Lys Val
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55
                                            60
Glu Asp Glu Tyr Arg Ala Phe Gln Glu Glu Ala Lys Lys Gln Ile Glu
                    70
                                        75
Asp Leu Asn Met Thr Leu Glu Lys Leu Arg Ser Asp Leu Asp Glu Lys
                85
                                    90
Glu Thr Glu Arg Ser Asp Met Lys Glu Thr Ile Phe Glu Leu Glu Asp
                                105
            100
                                                     110
Glu Val Glu Gln His Arg Ala Val Lys Leu His Asp Asn Leu Ile Ile
                                                125
                            120
Ser Asp Leu Glu Asn Thr Val Lys Lys Leu Gln Asp Gln Lys His Asp
                        135
Met Glu Arg Glu Ile Lys Thr Leu His Arg Arg Leu Arg Glu Glu Ser
                    150
                                         155
145
Ala Glu Trp Arg Gln Phe Gln Ala Asp Leu Gln Thr Ala Val Val Ile
                                    170
                165
Ala Asn Asp Ile Lys Ser Glu Ala Gln Glu Glu Ile Gly Asp Leu Lys
            180
                                185
                                                     190
Arg Arg Val His Glu Ala Gln Glu Lys Asn Glu Lys Leu Thr Lys Glu
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Leu Glu Glu Ile Ser Pro Pro Ser Gln Lys
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Asp Arg Thr Cys Asn Asn Glu Val Val Lys Met Gln Arg Leu Thr Leu
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Glu His Leu Asn Gln Met Val Gly Ile Glu Tyr Ile Leu Leu His Ala
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Gln Glu Pro Ile Leu Phe Ile Ile Arg Lys Gln Gln Arg Gln Ser Pro
Ala Gln Val Ile Pro Leu Ala Asp Tyr Tyr Ile Ile Ala Gly Val Ile
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                                    90
Tyr Gln Ala Pro Asp Leu Gly Ser Val Ile Asn Ser Arg Val Leu Thr
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            100
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Ala Val His Gly Ile Gln Ser Ala Phe Asp Glu Ala Met Ser Tyr Cys
                            120
Arg Tyr His Pro Ser Lys Gly Tyr Trp Trp His Phe Lys Asp His Glu
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                                            140
Glu Gln Asp Lys Val Arg Pro Lys Ala Lys Arg Lys Glu Glu Pro Ser
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Ser Ile Phe Gln Arg Gln Arg Val Asp Ala Leu Leu Leu Asp Leu Arg
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                                    170
Gln Lys Phe Pro Pro Lys Phe Val Gln Leu Lys Pro Gly Glu Lys Pro
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                                185
                                                    190
Val Gln Val Asp Gln Thr Lys Lys Glu Ala Glu Pro Ile Pro Glu Thr
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Val Lys Pro Glu Glu Lys Glu Thr Pro Glu Cys Thr Thr Arg Pro Gly
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Val Leu Lys Ala Pro Leu Lys Asn Gly
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<211> 449

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<400> 146

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Leu 145	Glu	Ser	Pro	Asp	Phe 150	Gln	Pro	Asn	Ile	Ala 155	Lys	Lys	Tyr	Ile	Asp 160
	Lys	Phe	Val	Leu 165	Gln	Leu	Leu	Glu	Leu 170	Phe	Asp	Ser	Glu	Asp 175	Pro
Arg	Glu	Arg	Asp 180	Phe	Leu	Lys	Thr	Thr 185	Leu	His	Arg	Ile	Tyr 190	Gly	Lys
Phe	Leu	Gly 195	Leu	Arg	Ala	Tyr	Ile 200	Arg	Lys	Gln	Ile	Asn 205	Asn	Ile	Phe
Tyr	Arg 210	Phe	Ile	Tyr	Glu	Thr 215	Glu	His	His	Asn	Gly 220	Ile	Ala	Glu	Leu
Leu 225	Glu	Ile	Leu	Gly	Ser 230	Ile	Ile	Asn	Gly	Phe 235	Ala	Leu	Pro	Leu	Lys 240
Glu	Glu	His	Lys	Ile 245	Phe	Leu	Leu	Lys	Val 250	Leu	Leu	Pro	Leu	His 255	Lys
Val	Lys	Ser	Leu 260	Ser	Val	Tyr	His	Pro 265	Gln	Leu	Ala	Tyr	Cys 270	Val	Val
Gln	Phe	Leu 275	Glu	Lys	Asp	Ser	Thr 280	Leu	Thr	Glu	Pro	Val 285	Val	Met	Ala
Leu	Leu 290	Lys	Tyr	Trp	Pro	Lys 295	Thr	His	Ser	Pro	Lys 300	Glu	Val	Met	Phe
Leu 305	Asn	Glu	Leu	Glu	Glu 310	Ile	Leu	Asp	Val	Ile 315	Glu	Pro	Ser	Glu	Phe 320
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Ser	Pro	His	Phe	Gln	Val	Ala	Glu	Arg 345	Ala	Leu	Tyr	Tyr	Trp 350	Asn	Asn
Glu	Tyr	Ile 355	Met	Ser	Leu	Ile	Ser 360	Asp	Asn	Ala	Ala	Lys 365	Ile	Leu	Pro
Ile	Met 370	Phe	Pro	Ser	Leu	Tyr 375	Arg	Asn	Ser	Lys	Thr 380	His	Trp	Asn	Lys
Thr 385	Ile	His	Gly	Leu	Ile 390	Tyr	Asn	Ala	Leu	Lys 395	Leu	Phe	Met	Glu	Met 400
Asn	Gln	Lys	Leu	Phe 405	Asp	Asp	Cys	Thr	Gln 410	Gln	Phe	Lys	Ala	Glu 415	Lys
Leu	Lys	Glu	Lys 420	Leu	Lys	Met	Lys	Glu 425	Arg	Glu	Glu	Ala	Trp 430	Val	Lys
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Thr															

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<212> DNA

<213> Homo Sapiens

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<210> 148

<211> 500

<212> PRT

<213> Homo Sapiens

<400> 148

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230
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Tyr Ile His Tyr Gly Gln Thr Cys Lys Leu Val Cys Ser Val Thr Gly
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Met Ala Leu Pro Arg Leu Ile Ile Met Lys Val Asp Lys His Thr Ala
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                                265
Leu Leu Asp Ala Asp Pro Val Ser Gln Leu His Lys Cys Ala Phe
                           280
                                                285
Tyr Leu Lys Asp Thr Glu Arg Met Tyr Leu Cys Leu Ser Gln Glu Arg
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Ile Ile Gln Phe Gln Ala Thr Pro Cys Pro Lys Glu Pro Asn Lys Glu
                    310
                                        315
Met Ile Asn Asp Gly Ala Ser Trp Thr Ile Ile Ser Thr Asp Lys Ala
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                                    330
Glu Tyr Thr Phe Tyr Glu Gly Met Gly Pro Val Leu Ala Pro Val Thr
                             345
Pro Val Pro Val Val Glu Ser Leu Gln Leu Asn Gly Gly Gly Asp Val
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                           360
                                                365
Ala Met Leu Glu Leu Thr Gly Gln Asn Phe Thr Pro Asn Leu Arg Val
                        375
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Trp Phe Gly Asp Val Glu Ala Glu Thr Met Tyr Arg Cys Gly Glu Ser
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                                        395
Met Leu Cys Val Val Pro Asp Ile Ser Ala Phe Arg Glu Gly Trp Arg
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Trp Val Arg Gln Pro Val Gln Val Pro Val Thr Leu Val Arg Asn Asp
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                                425
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Gly Ile Ile Tyr Ser Thr Ser Leu Thr Phe Thr Tyr Thr Pro Glu Pro
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                                                445
Gly Pro Arg Pro His Cys Ser Val Ala Gly Ala Ile Leu Pro Ala Asn
                        455
Ser Ser Gln Val Pro Pro Asn Glu Ser Asn Thr Asn Ser Glu Gly Ser
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Thr Val Val Ser
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gacaaggagc gggtcgcgct ggtggtgcac ccgggcacgg cacggctggg gagcccggac
                                                                      180
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gtecaggagt tggagaaaca gcaggtcacc atcctggcca cgccccttcc cgaggagagc
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atgaagcagg agctgcagaa cctgcgcgat gagatcaaac agctggggag ggagatccgc
                                                                      360
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                                                                      420
aacacaagaa tgagaaaaac ccagcatggg gtcctgtccc agcaattcgt ggagctcatc
                                                                      480
aacaagtgca attcaatgca gtccgaatac cgggagaaga acgtggagcg gattcggagg
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cagetgaaga teaceaatge tggeatggtg tetgatgagg agttggatea gatgetggae
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agtgggcaaa gegaggtgtt tgtgteeaat ateettaagg acaegeaggt gactegaeag
                                                                      660
gccttaaatg agatetegge eeggcacagt gagatecage agettgaacg eagtattegt
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780

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Arg Leu Gly	Ser Pro	Asp Glu	Glu 40	Phe	Phe	His	Lys	Val 45	Arg	Thr	Ile
Arg Gln Thr 50	Ile Val	Lys Leu 55	Gly	Asn	Lys	Val	Gln 60	Glu	Leu	Glu	Lys
Gln Gln Val 65	Thr Ile	Leu Ala	Thr	Pro	Leu	Pro 75	Glu	Glu	Ser	Met	Lys 80
Gln Glu Leu	Gln Asn 85	Leu Arg	Asp	Glu	Ile 90		Gln	Leu	Gly	Arg 95	
Ile Arg Leu		Lys Ala	Ile	Glu 105	-	Gln	Lys	Glu	Glu 110		Asp
Glu Asn Tyr 115		Val Asn	Thr 120		Met	Arg	Lys	Thr 125		His	Gly
Val Leu Ser	Gln Gln	Phe Val	Glu	Leu	Ile	Asn	Lys 140		Asn	Ser	Met
Gln Ser Glu	Tyr Arg	Glu Lys		Val	Glu			Arg	Arg	Gln	
145 Lys Ile Thr	Asn Ala	150 Gly Met	Val	Ser	Asp	155 Glu	Glu	Leu	Asp	Gln	160 Met
Leu Asp Ser	165 Gly Gln		Val	Phe	170 Val	Ser	Asn	Ile	Leu	175 Lys	Asp
	180		_	185			_		190		_
Thr Gln Val	Thr Arg	Gin Ala	Lеи 200	Asn	GIU	IIe	ser	A1a 205	Arg	His	Ser
Glu Ile Gln 210	Gln Leu	Glu Arg 215		Ile	Arg	Glu	Leu 220	His	Aap	Ile	Phe
Thr Phe Leu	Ala Thr		Glu	Met	Gln	•	Glu	Met	Ile	Asn	•
225 Ile Glu Lys	Asn Tle	230 Leu Ser	Ser	Δla	Δsn	235 Tvr	Val	Glu	Ara	Glv	240 Gln
_	245				250					255	
Glu His Val	Lys Thr 260	Ala Leu	Glu	Asn 265	Gln	Lys	Lys	val	Arg 270	Lys	ràa
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Glu Ser Glu Glu Val Val Ser Arg Glu Val Ser Gly Ile Lys Ala Ala

65

Tyr Glu Ala Glu Leu Gly Asp Ala Arg Lys Thr Leu Asp Ser Val Ala 90 Lys Glu Arg Ala Arg Leu Gln Leu Glu Leu Ser Lys Val Arg Glu Glu 105 Phe Lys Glu Leu Lys Ala Arg Asn Thr Lys Lys Glu Gly Asp Leu Ile 120 Ala Ala Gln Ala Arg Leu Lys Asp Leu Glu Ala Leu Leu Asn Ser Lys 135 Glu Ala Ala Leu Ser Thr Ala Leu Ser Glu Lys Arg Thr Leu Glu Gly 150 155 Glu Leu His Asp Leu Arg Gly Gln Val Ala Lys Leu Glu Ala Ala Leu 170 Gly Glu Ala Lys Lys Gln Leu Gln Asp Glu Met Leu Arg Arg Val Asp 185 Ala Glu Asn Arg Leu Gln Thr Met Lys Glu Glu Leu Asp Phe Gln Lys 200 Asn Ile Tyr Ser Glu Glu Leu Arg Glu Thr Lys Arg Arg His Glu Thr 215 220 Arg Leu Val Glu Ile Asp Asn Gly Lys Gln Arg Glu Phe Glu Ser Arg 230 235 Leu Ala Asp Ala Leu Gln Glu Leu Arg Ala Gln His Glu Asp Gln Val 245 250 Glu Gln Tyr Lys Lys Glu Leu Glu Lys Thr Tyr Ser Ala Lys Leu Asp 265 Asn Ala Arg Gln Ser Ala Glu Arg Asn Ser Asn Leu Val Gly Ala Ala 280 His Glu Glu Leu Gln Gln Ser Arg Ile Arg Ile Asp Ser Leu Ser Ala 295 Gln Leu Ser Gln Leu Gln Lys Gln Leu Ala Ala Lys Glu Ala Lys Leu 310 315 Arg Asp Leu Glu Asp Ser Leu Ala Arg Glu Arg Asp Thr Ser Arg Arg 330 Leu Leu Ala Glu Lys Glu Arg Glu Met Ala Glu Met Arg Ala Arg Met 345 Gln Gln Gln Leu Asp Glu Tyr Gln Glu Leu Leu Asp Ile Lys Leu Ala 360 365 Leu Asp Met Glu Ile His Ala Tyr Arg Lys Leu Leu Glu Gly Glu Glu 375 Glu Arg Leu Arg Leu Ser Pro Ser Pro Thr Ser Gln Arg Ser Arg Gly 390 395 Arg Ala Ser Ser His Ser Ser Gln Thr Gln Gly Gly Ser Val Thr 405 410 Lys Lys Arg Lys Leu Glu Ser Thr Glu Ser Arg Ser Ser Phe Ser Gln 420 425 His Ala Arg Thr Ser Gly Arg Val Ala Val Glu Glu Val Asp Glu Glu 440 Gly Lys Phe Val Arg Leu Arg Asn Lys Ser Asn Glu Asp Gln Ser Met 455 Gly Asn Trp Gln Ile Lys Arg Gln Asn Gly Asp Asp Pro Leu Leu Thr 470 475 Tyr Arg Phe Pro Pro Lys Phe Thr Leu Lys Ala Gly Gln Val Val Thr 490 Ile Trp Ala Ala Gly Ala Gly Ala Thr His Ser Pro Pro Thr Asp Leu 505 Val Trp Lys Ala Gln Asn Thr Trp Gly Cys Gly Asn Ser Leu Arg Thr

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Gln	Glu	Met	Gly		Glu	Asn	Ala	Glu		Thr	Glu	Glu	Met		Asp
			100	_				105					110		-
Gln	Ala		Asp	Lys	Lys	Val		Ala	Ile	Glu	Ala		Asn	Asp	Gly
C1.,	T 011	115	Tara	77.	Tla	7.00	120	Dho	mb~	7	77.	125	T	T	3
Giu	Leu 130	GIII	ьуѕ	AIA	TTE	135	Leu	Pne	IIII	Asp	140	TIE	гуѕ	Leu	ASII
Pro	Arg	Leu	Ala	Ile	Leu		Ala	Lys	Arg	Ala		Val	Phe	Val	Lys
145	_				150	_		_	_	155					160
Leu	Gln	Lys	Pro		Ala	Ala	Ile	Arg		Cys	Asp	Arg	Ala		Glu
T1_	7. ~~~	Dwa	7	165	71-	<b>a</b> 1-	D	m	170	<b></b>	<b>3</b>	<b>a</b> 1	<b>T</b>	175	***
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Arg	Leu	Leu		His	Trp	Glu	Glu		Ala	His	Asp	Leu		Leu	Ala
		195	_		-		200				_	205			
Cys	Lys	Leu	Asp	Tyr	Asp		Asp	Ala	Ser	Ala		Leu	Lys	Glu	Val
C1 n	210	λ ».«	71-	<b>~1</b> ~	T * * *	215	71-	<b>a</b> 1	77 d =	7	220	T	<b></b>	<b>61</b>	<b>3</b>
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	Arg	Glu	Glu	Arg		Ile	Lys	Glu	Arg		Glu	Arg	Val	Lys	
				245					250					255	-
Ala	Arg	Glu		His	Glu	Arg	Ala		Arg	Glu	Glu	Glu		Arg	Arg
Gln	Ser	Glv	260 21a	G] n	ጥኒም	Glv	Sar	265 Dhe	Dro	Glv	Glaz	Dhe	270 Bro	Gly	C111
GIII	261	275	AIa	GIII	TAT	GIY	280	FIIC	PIO	GLY	Gry	285	PIO	GIY	GIY
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	Gly	Met	Ala	Gly		Pro	Gly	Leu	Asn		Ile	Leu	Ser	Asp	
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O.L.	vu	200	7114	325	1100	GIII	ASP	110	330	Vai	riec	vai	AIA	335	GIII
Asp	Val	Ala	Gln	Asn	Pro	Ala	Asn	Met	Ser	Lys	Tyr	Gln	Ser		Pro
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<212> DNA

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cagtaaagaa agaaatccag agaggaagga agttgaaatg caaattttgt cataaaagag 360
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480

540

600

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720

780

840

900

960

1020

1080

1140

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1260

1320

1323

60

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Asn Pro Asp Arg Ser Phe Asp Val Glu Ser Val Lys Lys Glu Ile Gln
Arg Gly Arg Lys Leu Lys Cys Lys Phe Cys His Lys Arg Gly Ala Thr
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                                        75
Val Gly Cys Asp Leu Lys Asn Cys Asn Lys Asn Tyr His Phe Phe Cys
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                                    90
Ala Lys Lys Asp Asp Ala Val Pro Gln Ser Asp Gly Val Arg Gly Ile
            100
Tyr Lys Leu Cys Gln Gln His Ala Gln Phe Pro Ile Ile Ala Gln
                            120
                                                125
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                        135
                                            140
Leu Ser Gly Asn His Val Gln Pro Pro Glu Thr Met Lys Cys Asn Thr
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                                        155
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